MEDICINSKI FAKULTET
Adresa: Kruševac bb
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Tel: +382 20 246 651
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UCG
Univerzitet Crne Gore

MEDICAL FACULTY
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MONTENEGRO
Phone: +382 20 246 651
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E-mail: infomedf@ac.me

Broj: 1819/12-1
Podgorica, 23.11.2023. godine

Univerzitet Crne Gore
Odbor za doktorske studije
n/r predsjedniku – prof. dr Borisu Vukićeviću

Poštovani,

U skladu sa članom 41 i 55 Pravila doktorskih studija, i tačkom 3.8. Vodiča za doktorske studije, u prilogu akta dostavljamo obrazac D2 (na službenom i engleskom jeziku) uz Predlog Odluke Vijeća o imenovanju Komisije za ocjenu doktorske disertacije dr med Isidore Rovčanin Dragović, pod nazivom „Nova metoda za stratifikovanje rizika za obolijevanje od Alchajmerove bolesti kod pacijenata u Crnoj Gori" sa pratećom dokumentacijom.

S poštovanjem.

MEDICINSKI FAKULTET
D E K A N,
Prof. dr Miodrag Radunović

ISPUNJENOST USLOVA DOKTORANDA

OPŠTI PODACI O DOKTORANDU			
Titula, ime, ime roditelja, prezime	Dr med. Isidora Rovčanin Dragović		
Fakultet	Medicinski fakultet		
Studijski program	Medicina		
Broj indeksa	1/13		
NAZIV DOKTORSKE DISERTACIJE			
Na službenom jeziku	Nova metoda za stratifikovanje rizika za obolijevanje od Alchajmerove bolesti kod pacijenata u Crnoj Gori		
Na engleskom jeziku	A new method for stratification of the risk for Alzheimer s disease in patients in Montenegro		
Naučna oblast	Translacione neuronauke		
MENTOR/MENTORI			
Prvi mentor	Prof. dr Nataša Popović	Medicinski fakultet Univerziteta Crne Gore	Fiziologija
Drugi mentor	Prof. dr Milica Martinović	Medicinski fakulteta Univerziteta Crne Gore	Patološka fiziologija
KOMISIJA ZA PREGLED I OCJENU DOKTORSKE DISERTACIJE			
Prof. dr Miodrag Radunović, redovni profesor		Medicinski fakultet Podgorica Univerzitet Crne Gore	Hepatobilijarna hirurgija
Prof. dr Nataša Popović, vanredna profesorica		Medicinski fakultet Univerziteta Crne Gore	Fiziologija
Prof. dr Milica Martinović, redovna profesorica		Medicinski fakultet Univerziteta Crne Gore	Patološka fiziologija
Prof. dr Elka Stefanova, redovna profesorica		Medicinskog fakulteta Univerziteta u Beogradu	Neurologija
Dr Apollonia Tullo, viši istraživač		Institut za biomebrane , bioenergetiku i molekularnu biotehnologiju, Nacionalni istraživački savjet, Bari, Italija	Molekularna biologija
Datum značajni za ocjenu doktorske disertacije			

Sjednica Senata na kojoj je data saglasnost na ocjenu temu i kandidata	21.01.2021.godine
Dostavljanja doktorske disertacije organizacionoj jedinici i saglasanost mentora	05.09.2023.godine
Sjednica Vijeća organizacione jedinice na kojoj je dat predlog za imenovanje komisija za pregled i ocjenu doktorske disertacije	16.11.2023. godine

ISPUNJENOST USLOVA DOKTORANDA

U skladu sa članom 38 Pravila doktorskih studija kandidat **je** dio sopstvenih istraživanja vezanih za doktorsku disertaciju publikovao u časopisu sa **(SCI/SCIE)/(SSCI/A&HCI)** liste kao prvi autor.

Spisak radova doktoranda iz oblasti doktorskih studija koje je publikovao u časopisima sa SCI /SCIE .

1. **Rovčanin Dragović I**, Popović N, Ždralević M, Radulović L, Vuković T, Marzano F, et al. Inflammation-related microRNAs-146a and -155 are upregulated in mild cognitive impairment subjects among older age population in Montenegro. Journal of Alzheimer's Disease. 2022;90:625–38.
Izdavač: IOS Press BV, Netherlands
doi:10.3233/jad-220676 (Impact Factor=4, SCIE, Q1)

2. Popovic N, Ždralević M, Vujosevic S, Radunović M, Zečević AA, **Dragović IR**, et al. Retinal microvascular complexity as a putative biomarker of biological age – a pilot study. 2023;
Izdavač: Springer Netherlands
doi:10.21203/rs.3.rs-2919375/v1 (Impact Factor= 4.28, SCIE, Q1)

3. Ždralević M, Raonić J, Popovic N, Vučković L, **Rovčanin Dragović I**, Vukčević B, et al. The role of miRNA in colorectal cancer diagnosis: A pilot study. Oncology Letters. 2023;25.
Izdavač: Spandidos Publications Greece
doi:10.3892/ol.2023.13853 (Impact Factor= 3.11, SCIE, Q3)

Obrazloženje mentora o korišćenju doktorske disertacije u publikovanim radovima

Doktorska disertacija je jedan od glavnih ishoda naučno-istraživačkog projekta pod nazivom „Nove metode za stratifikaciju rizika za progresiju kancera i Alchajmerove bolesti kod pacijenata u Crnoj Gori" (DEMONSTRATE). Projekat je finansiran od stane Ministarstva nauke Crne Gore (Grant br. 01-781/02). Shodno tome, dio istraživačkog materijala koji proističe kako iz doktorske disertacije, tako i iz projekta DEMONSTRATE, publikovan je u sljedećim radovima:

1. **Rovčanin Dragović I**, Popović N, Ždralević M, Radulović L, Vuković T, Marzano F, et al. Inflammation-related micrornas-146a and -155 are upregulated in mild cognitive impairment subjects among older age population in Montenegro. Journal of Alzheimer's Disease. 2022;90:625–38.
Izdavač: IOS Press BV, Netherlands
doi:10.3233/jad-220676 (Impact Factor=4, SCIE, Q1)

2. Popovic N, Ždralević M, Vujosevic S, Radunović M, Zečević AA, **Dragović IR**, et al. Retinal microvascular complexity as a putative biomarker of biological age – a pilot study. 2023;
Izdavač: Springer Netherlands
doi:10.21203/rs.3.rs-2919375/v1 (Impact Factor= 4.28, SCIE, Q1)

3. Ždralević M, Raonić J, Popovic N, Vučković L, **Rovčanin Dragović I**, Vukčević B, et al. The role of MIRNA in colorectal cancer diagnosis: A pilot study. Oncology Letters. 2023;25.
Izdavač: Spandidos Publications Greece
doi:10.3892/ol.2023.13853 (Impact Factor= 3.11, SCIE, Q3)

Svaki od navedenih radova je prošao recenziju od strane nezavisne komisije sastavljene od eminentnih internacionalno priznatih stručnjaka iz odgovarajuće naučne oblasti (Journal of Alzheimer's Disease - Medicina, Psihijatrija i Mentalno zdravlje; Biogerontology - Gerontologija (naučna grana koja proučava fiziologiju starenja); Oncology Letters- Onkologija).
Pomenute komisije su ocijenile ishode istraživanja kao značajan dodatak kvantumu znanja i potvrdile da rezultati zaslužuju da budu objavljeni u odgovoarajućim internacionalnim naučnim časopisima. Važno je napomenuti da ovi časopisi pokrivaju široki diapazon naučnih oblasti u okviru fiziologije i medicine: od fiziologije starenja, preko Alchajmerove bolesti do onkoloških oboljenja. Ova raznovrsnost dodatno potvrđuje univerzalnost i široku primjenjivost novog znanja koje je proizišlo iz rezultata izloženih u doktorskoj disertaciji, i svedoči izuzetnom značaju ovog istraživanja.

Datum i ovjera (pečat i potpis odgovorne osobe)

U Podgorici ,
(16.11.2023. godine)

MP

DEKAN
Prof. dr Miodrag Radunović

Prilog dokumenta sadrži:

1. Potvrdu o predaji doktorske disertacije organizacionoj jedinici
2. Odluku o imenovanju komisije za pregled i ocjenu doktorske disertacije
3. Kopiju rada publikovanog u časopisu sa odgovarajuće liste
4. Biografiju i bibliografiju kandidata
5. Biografiju i bibliografiju članova komisije za pregled i ocjenu doktorske disertacije sa potvrdom o izboru u odgovarajuće akademsko zvanje i potvrdom da barem jedan član komisije nije u radnom odnosu na Univerzitetu Crne Gore

FULFILLMENTS OF THE REQUIREMENTS OF THE DOCTORAL STUDENT

GENERAL DATA ABOUT THE DOCTORAL STUDENT			
Name, name of the parent, surname, title	Isidora, Rade, Rovčanin Dragović, MD		
Faculty	Faculty of Medicine		
Study program	Medicine		
Broj indeksa	1/13		
TITLE OF DOCTORAL DISSERTATION			
In the official language	Nova metoda za stratifikovanje rizika za obolijevanje od Alchajmerove bolesti kod pacijenata u Crnoj Gori		
In English language	A new method for stratification of the risk for Alzheimer's disease in patients in Montenegro		
Scientific field	Translational Neuroscience		
MENTOR/MENTORS			
The first mentor	Prof. Dr. Nataša Popović	Faculty of Medicine of the University of Montenegro	Physiology
The second mentor	Prof. Dr. Milica Martinović	Faculty of Medicine of the University of Montenegro	Pathological Physiology
DOCTORAL DISSERTATION REVIEW AND ASSESSMENT COMMITTEE			
Prof. Dr. Miodrag Radunović, Full Professor		Faculty of Medicine of the University of Montenegro	Hepatobiliary surgery
Prof. Dr. Nataša Popović, Associate Professor		Faculty of Medicine of the University of Montenegro	Physiology
Prof. Dr. Milica Martinović, Full Professor		Faculty of Medicine of the University of Montenegro	Pathological Physiology
Prof. Dr. Elka Stefanova, Full Professor		Faculty of Medicine of the University in Belgrade	Neurology
Dr. Apollonia Tullo, Senior Researcher		Institute of Biomembranes, Bioenergetics and Molecular Biotechnologies, Department of Biomedical Sciences, National Research Council, Bari.	Molecular Biology
Dates important for the evaluation of the Doctoral Dissertation			

Senate session at which consent was given to the evaluation of the topic and the candidate	01.21.2021.
Submission of the Doctoral Dissertation to the organizational unit and consent of the mentors	09.05.2023.
The meeting of the Council of the organizational unit at which the proposal was made for the appointment of a Committee for the review and evaluation of the Doctoral Dissertation	16.11.2023.

FULFILLMENT OF THE REQUIREMENTS OF THE DOCTORAL STUDENT

In accordance with the Article 38 of the Rules of Doctoral Studies, the candidate has published part of their own research related to the Doctoral Dissertation in a journal on the (SCI/SCIE)/(SSCI/A&HCI) list as the first author.

List of scientific papers of the doctoral student in the field of Doctoral Studies published in SCI/SCIE journals.

1. **Rovčanin Dragović I**, Popović N, Ždralević M, Radulović L, Vuković T, Marzano F, et al. Inflammation-related microRNAs-146a and -155 are upregulated in mild cognitive impairment subjects among older age population in Montenegro. Journal of Alzheimer's Disease. 2022;90:625–38.
Publisher: IOS Press BV, Netherlands
doi:10.3233/jad-220676 (Impact Factor=4, SCIE, Q1)

2. Popovic N, Ždralević M, Vujosevic S, Radunović M, Zečević AA, **Dragović IR**, et al. Retinal microvascular complexity as a putative biomarker of biological age – a pilot study. 2023;
Publisher: Springer Netherlands
doi:10.21203/rs.3.rs-2919375/v1 (Impact Factor= 4.28, SCIE, Q1)

3. Ždralević M, Raonić J, Popovic N, Vučković L, **Rovčanin Dragović I**, Vukčević B, et al. The role of miRNA in colorectal cancer diagnosis: A pilot study. Oncology Letters. 2023;25.
Publisher: Spandidos Publications Greece
doi:10.3892/ol.2023.13853 (Impact Factor= 3.11, SCIE, Q3)

Rationale of the mentor about the use of Doctoral Dissertation in published papers

The doctoral dissertation is one of the main outcomes of the scientific research project named „New methods for the stratification of the risk for progression of cancer and Alzheimer's disease in patients in Montenegro" (DEMONSTRATE). The project was financed by the Ministry of Science of Montenegro (Grant No. 01-781/02). Accordingly, a part of the research material that stems from both, the doctoral dissertation and the DEMONSTRATE project, was published in the following papers:

1. **Rovčanin Dragović I**, Popović N, Ždralević M, Radulović L, Vuković T, Marzano F, et al. Inflammation-related micrornas-146a and -155 are upregulated in mild cognitive impairment subjects among older age population in Montenegro. Journal of Alzheimer's Disease. 2022;90:625–38.
Publisher: IOS Press BV, Netherlands
doi:10.3233/jad-220676 (Impact Factor=4, SCIE, Q1)

2. Popovic N, Ždralević M, Vujosevic S, Radunović M, Zečević AA, **Dragović IR**, et al. Retinal microvascular complexity as a putative biomarker of biological age – a pilot study. 2023; Publisher: Springer Netherlands
doi:10.21203/rs.3.rs-2919375/v1 (Impact Factor= 4.28, SCIE, Q1)

3. Ždralević M, Raonić J, Popovic N, Vučković L, **Rovčanin Dragović I**, Vukčević B, et al. The role of MIRNA in colorectal cancer diagnosis: A pilot study. Oncology Letters. 2023;25.
Publisher: Spandidos Publications Greece
doi:10.3892/ol.2023.13853 (Impact Factor= 3.11, SCIE, Q3)

Each of the above-mentioned papers has been peer-reviewed by an independent committee composed of eminent internationally recognized experts from the respective scientific field (Journal of Alzheimer's Disease - Medicine, Psychiatry and Mental Health; Biogerontology - Gerontology; Oncology Letters - Oncology). The aforementioned commissions evaluated the research results and decided that they represent a significant addition to the quantum of knowledge, confirming that these results deserve to be published in relevant international scientific journals. It is important to note that these journals cover a wide range of scientific fields within Physiology and Medicine: from the physiology of aging, through Alzheimer's disease to oncological diseases. This diversity additionally confirms the universality and broad applicability of the new knowledge that emerged from the results presented in the Doctoral Dissertation, and testifies to the exceptional importance of this research.

Date and certification (stamp and signature of the responsible person)

In Podgorica,
(16.11.2023.)

UNIVERZITET CRNE GORE UCG MP

DEAN
Prof. Dr. Miodrag Radunović

The attachment of the document contains:

1. Confirmation of the submission of the Doctoral Dissertation to the organizational unit.
2. Decision on the appointment of the Committee for the review and evaluation of the Doctoral Dissertation.
3. A copy of the work published in the journal from the corresponding list.
4. Biography and bibliography of the candidate.
5. Biography and bibliography of the Committee for the review and evaluation of the doctoral dissertation with confirmation of election to the appropriate academic title and confirmation that at least one member of the Committee is not employed at the University of Montenegro.

UNIVERZITET CRNE GORE

MEDICINSKI FAKLTET

Broj: 1179/1-1

Podgorica 06.10.2023. godine

P O T V R D A

Potvrđuje se da je dr med Isidora Rovčanin Dragović , predala 7 primjeraka doktorske disertacije, pod nazivom **„ Nova metoda za stratifikovanje rizika za obolijevanje od Alchajmerove bolesti kod pacijenata u Crnoj Gori " dana 05.09.2023**.godine .

Potvrda se izdaje u svrhu pregleda i ocjene doktorske disrtacije.

ŠEF STUDENTSKE SLUŽBE

Sonja Vukićević, diplomirani pravnik

UNIVERZITET CRNE GORE
MEDICINSKI FAKULTET
Primljeno: 05.09.2023

Org. jed.	Broj	Prilog	Vrijednost
med	1179		

UNIVERZITET CRNE GORE

Vijeću Medicinskog fakulteta

Komisiji za doktorske studije

PREDMET: Zahtjev za ocjenu doktorske disertacije

Poštovani,

U skladu sa Pravilima studiranja na doktorskim studijama Univerziteta Crne Gore, ovim putem podnosim zahtjev za ocjenu doktorske disertacije pod nazivom:

„Nova metoda za stratifikovanje rizika za obolijevanje od Alchajmerove bolesti kod pacijenata u Crnoj Gori"

Završetkom doktorske disertacije i objavom rada u časopisu sa SCI/SCIE liste koji sadrži djelove sopstvenih istraživanja sprovedenih u okviru izrade doktorske disertacije, ispunila sam uslove za predaju disertacije na pregled i ocjenu, predviđene Pravilima doktorskih studija Univerziteta Crne Gore.

Ovim putem se obraćam Komisiji za doktorske studije Medicinskog fakulteta, sa molbom da inicira predlog Komisije za ocjenu gore navedene doktorske disertacije.

Uz Zahtjev, u prilogu dostavljam sljedeće:

- Pismenu saglasnost mentora i komentora
- Sedam primjeraka doktorske disertacije (u štampanoj formi)
- Fotokopiju rada objavljenog u časopisu sa SCI/SCIE liste koji sadrži dio rezultata iz doktorske disertacije
- Biografiju i bibliografiju
- CD sa cjelokupnim sadržajem doktorske disertacije u PDF formatu i objavljenim radom
- Potpisanu izjavu o autorstvu i istovjetnosti štampane i elektronske verzije doktorskog rada (Prilog 1 i 2 iz Uputstva o oblikovanju doktorske disertacije)

S poštovanjem,

Dr med. Isidora Rovčanin Dragović

U Podgorici,

UNIVERSITY OF MONTENEGRO

Council of the Faculty of Medicine

Commission for Doctoral Studies

OBJECT: Application for the evaluation of the Doctoral Dissertation

In accordance with the Rules of studying at Doctoral studies of the University of Montenegro, I hereby submit an application for the evaluation of the Doctoral Dissertation, entitled:

„A new method for stratification of the risk for Alzheimer's disease in patients in Montenegro"

By completing the Doctoral Dissertation and publishing a paper in a journal from the SCI/SCIE list, containing parts of my own research, conducted within the framework of the preparation of the Doctoral Dissertation, I have fulfilled the conditions for submitting my Dissertation for examination and evaluation, as envisaged by the Rules of Doctoral Studies of the University of Montenegro.

I hereby address the Commission for Doctoral Studies of the Faculty of Medicine, with a request to initiate the proposal for the evaluation of the above-mentioned Doctoral Dissertation.

In addition to the Request, I submit the following in the annex:

- Written consent of mentor and comentor
- Seven copies of the Doctoral Dissertation (in printed form)
- A photocopy of the paper published in a journal indexed in the SCI/SCIE list containing part of the results from the Doctoral Dissertation
- Biography and bibliography
- CD with the entire content of the Doctoral Dissertation in PDF format and published paper
- Signed statement on authorship and equivalence of the printed and electronic versions of the Doctoral Dissertation (Attachments 1 and 2 from the Instruction on the design of the Doctoral Dissertation)

Sincerely,

Isidora Rovčanin Dragović, MD

In Podgorica,

UNIVERZITET CRNE GORE

MEDICINSKI FAKULTET

Na osnovu Odluka Senata Univerziteta Crne Gore broj: 03-2154/2 i 03-3390/6-2016 imenovane smo za mentora i komentora za izradu doktorske disertacije, kandidatkinje dr med Isidore Rovčanin Dragović. U fazi predaje doktorske disertacije na pregled i ocjenu, u skladu sa Pravilima doktorskih studija Univerziteta Crne Gore, dajemo

S A G L A S N O S T

Saglasne smo da kandidatkinja dr med Isidora Rovčanin Dragović može predati doktorsku disertaciju pod nazivom **„Nova metoda za stratifikovanje rizika za obolijevanje od Alchajmerove bolesti kod pacijenata u Crnoj Gori“** na pregled i ocjenu.

S poštovanjem,

U Podgorici, 01.09.2023. godine

Mentor

Prof. dr Nataša Popović

Komentor

Prof. dr Milica Martinović

UNIVERSITY OF MONTENEGRO

FACULTY OF MEDICINE

Based on the Decision of the Senate of the University of Montenegro, no.: 03-2154/2 and 03-3390/6-2016 we have been appointed as a mentor and co-mentor for the preparation of the doctoral dissertation, of the candidate Isidora Rovčanin Dragović, MD. In the phase of submitting the doctoral dissertation for review and evaluation, in accordance with the Rules of Doctoral Studies of the University of Montenegro, we give

C O N S E N T

We agree that the PhD candidate Isidora Rovčanin Dragović, can submit a doctoral dissertation under the title: " A new method for stratification of the risk for Alzheimer's disease in patients in Montenegro", for review and evaluation.

Sincerely,

In Podgorica, September 1st 2023.

Mentor

Prof. Dr. Nataša Popović

Co - mentor

Prof. Dr. Milica Martinović

UNIVERZITET CRNE GORE
MEDICINSKI FAKULTET
Broj: 1819/12
Podgorica, 16.11.2023. godine

Na osnovu člana 64 stav 1 tačka 9 Statuta Univerziteta Crne Gore, (Bilten UCG br.337/2015 i br 447/2018), člana 41 i 55 Pravila doktorskih studija, inicijalnog predloga Komisije za doktorske studije Medicinskog fakulteta broj: 1179/1 od 06.10.2023 godine i tačke 3.8 Vodiča za doktorske studije Univerziteta Crne Gore, Vijeće Medicinskog fakulteta na sjednici održanoj 16.11.2023. godine, donijelo je

O D L U K U

I

Kandidat dr med Isidora Rovčanin Dragović, ispunjava formalne uslove za ocjenu doktorske disertacije: **„Nova metoda za stratifikovanje rizika za obolijevanje od Alchajmerove bolesti kod pacijenata u Crnoj Gori".**

II

Predlaže se Komisija za ocjenu doktorske disertacije dr med Isidore Rovčanin Dragović, pod navedenim nazivom: **„Nova metoda za stratifikovanje rizika za obolijevanje od Alchajmerove bolesti kod pacijenata u Crnoj Gori"** u sastavu:

1. **Prof. dr Miodrag Radunović**, redovni profesor Medicinskog fakulteta Univerziteta Crne Gore, naučna oblast: hirurgija;
2. **Prof. dr Nataša Popović**, vanredna profesorica Medicinskog fakulteta Univerziteta Crne Gore, naučna oblast: medicinska fiziologija;
3. **Prof. dr Milica Martinović**, redovna profesorica Medicinskog fakulteta Univerziteta Crne Gore, naučna oblast: patološka fiziologija sa laboratorijskom medicinom;
4. **Prof. dr Elka Stefanova**, redovna profesorica Medicinskog fakulteta Univerziteta u Beogradu; naučna oblast: neurologija
5. **Dr Apollonia Tulo**, istraživač Instituta za biomembrane, bioenergetiku i molekularnu biotehnologiju, Bari, Italija, naučna oblast: molekularna biologija.

III

Komisija za ocjenu doktorske disertacije je dužna da Vijeću Medicinskog fakulteta, podnese izvještaj koji sadrži ocjenu doktorske disertacije.

Obrazloženje

Dr med Isidora Rovčanin Dragović je predala doktorsku disertaciju pod nazivom: **Nova metoda za stratifikovanje rizika za obolijevanje od Alchajmerove bolesti kod pacijenata u Crnoj Gori** " dana 05.09.2023_. godine.
Vijeće Medicinskog fakulteta je utvrdilo da kandidat ispunjava uslove iz člana 38 Pravila doktorskih studija, da kandidat dr med Isidora Rovčanin Dragović ima, kao prvi autor rad sa rezultatima iz teze objavljen u časopisu sa SCI/**SCIE** liste. Samim tim su se stekli uslovi da se imenuje Komisija za ocjenu pomenute doktorske disertacije. Na osnovu svega navedenog, odlučeno je kao u dispozitivu ove Odluke.

VIJEĆE MEDICINSKOG FAKULTETA
PREDSJEDAVAJUĆI,

Prof. dr Miodrag Radunović, dekan

Journal of Alzheimer's Disease 90 (2022) 625–638
DOI 10.3233/JAD-220676
IOS Press

Inflammation-Related microRNAs-146a and -155 Are Upregulated in Mild Cognitive Impairment Subjects Among Older Age Population in Montenegro

Isidora Rovčanin Dragović[a,*], Nataša Popović[a], Maša Ždralević[a], Ljiljana Radulović[b], Tijana Vuković[b], Flaviana Marzano[c], Apollonia Tullo[c] and Miodrag Radunović[a]
[a]*University of Montenegro, Faculty of Medicine, Podgorica, Montenegro*
[b]*Clinical Center of Montenegro, Department of Neurology, Podgorica, Montenegro*
[c]*Institute of Biomembranes, Bioenergetics and Molecular Biotechnologies, National Research Council, CNR, Bari, Italy*

Accepted 19 August 2022
Pre-press 19 September 2022

Abstract.
Background: Pathological and clinical features of Alzheimer's disease (AD) are in temporal discrepancy and currently accepted clinical tests provide the diagnosis decades after the initial pathophysiological events. In order to enable a more timely detection of AD, research efforts are directed to identification of biomarkers of the early symptomatic stage. Neuroinflammatory signaling pathways and inflammation-related microRNAs (miRNAs) could possibly have a crucial role in AD, making them promising potential biomarkers.
Objective: We examined the expression of circulatory miRNAs with a documented role in AD pathophysiology: miR-29a/b, miR-101, miR-125b, miR-146a, and miR-155 in the plasma of AD patients (AD, $n = 12$), people with mild cognitive impairment (MCI, $n = 9$), and normocognitive group (CTRL, $n = 18$). We hypothesized that these miRNA expression levels could correlate with the level of participants' cognitive decline.
Methods: The study participants completed the standardized interview, neurological examination, neuropsychological assessment, and biochemical analyses. miRNA expression levels were assessed by RT-PCR.
Results: Neurological and laboratory findings could not account for MCI, but miR-146a and -155 were upregulated in the MCI group compared to the control. miR-146a, known to mediate early neuroinflammatory AD events, was also upregulated in the MCI compared to AD group. ROC curve analysis for miRNA-146a showed 77.8% sensitivity and 94.4% specificity and 66.7% sensitivity and 88.9% specificity for miR-155.
Conclusion: Determination of circulatory inflamma-miRs-146a and -155 expression, together with neuropsychological screening, could become a non-invasive tool for detecting individuals with an increased risk for AD, but research on a larger cohort is warranted.

Keywords: Alzheimer's disease, mild cognitive impairment, miR-146a, miR-155, neuroinflammation

INTRODUCTION

Life expectancy has doubled in the world since the beginning of the 20th century, leading to an increased incidence of Alzheimer's disease (AD), as a disease of the elderly. AD is responsible for 60–70% of all dementia diagnoses [1]. Ninety-five percent

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of patients diagnosed with AD are sporadic cases and remaining 5% have familial gene mutations [2]. Among people who are 65 years and older, 10% are thought to have this progressive and ultimately fatal neurodegenerative disorder [1]. This global, increasing trend of AD is independent of their socio-economic status, and the financial burden due to AD is in range of cardiovascular diseases and carcinoma [3]. These facts identify AD as an insufficiently recognized problem, making the biomedical research in the dementia field a priority. In that regard, timely detection and slowing down of the disease course are of critical importance.

Difficulty of AD identification in a timely manner lies in the facts that pathological (AD-P) and clinical features (AD-C) of the disease are in temporal discrepancy and that clinical tests provide the diagnosis only when the first symptoms appear. Currently accepted biomarkers have relatively low specificity [4] and enable diagnosis sometimes even a few decades after the cascade of the pathophysiological processes has been initiated [5]. In addition, current treatments only alleviate symptoms, but do not have an effect on the causal mechanism, which has not yet been fully elucidated [6]. AD presents itself as the continuum from asymptomatic disease to dementia [7,8] and AD-C typically include incremental loss of memory and cognitive functions, involving the language, visuospatial, and executive domains [9]. However, at the beginning of the AD continuum, around 30% of individuals are estimated to have some level of AD-P, sometimes even significant brain changes, but no apparent symptoms [10]. Recently, the criteria for identification of subtle clinical manifestations prior to the objective evidence, subjective cognitive decline (SCD) due to AD, are structured and proposed as a useful concept [11]. However, there are still inconsistent and heterogeneous findings, regarding their clinical utility [12]. Therefore, the currently accepted diagnostic standard tools for an objective assessment [13] identify patients mainly in mild cognitive impairment (MCI) stage. A possibility of unambiguous clinical identification of this symptomatic AD stage, considered as early phase in the disease trajectory, make MCI a suitable ground for investigation of early pathological processes of the disease. Besides, the available data imply possibility to effectively slow down disease process in MCI stage, since there are cases of MCI which progress to dementia due to AD, but also those who remain stable over time [14]. Therefore, many research efforts are currently directed towards the identification of biomarkers of MCI stage. These biomarkers could not only contribute to the understanding of the early clinical stage itself and slowing down of the disease progress, but they could ultimately lead to AD diagnosis in preclinical stage and development of causative therapeutic modalities.

According to the results of the genetic studies of the early-onset familial forms of AD, irregular amyloid-β (Aβ) metabolism represents the initial molecular mechanism, ultimately leading to both AD-P and AD-C [15]. Currently, there are two biomarkers of extracellular Aβ accumulation: low cerebrospinal fluid (CSF) Aβ [16] and abnormal tracer retention on amyloid positron emission tomography (PET) imaging [17]. In addition, biomarkers of tau pathology [18] and biomarkers of neuronal injury in brain regions typical for AD [19] are also included in AD diagnostic guidelines [17]. The amyloid cascade, which has been proposed as the leading AD mechanism, might be very early pathophysiological event of the disease [20], but it is probably not the primary causative mechanism [21, 22,] and certainly, it does not offer enough explanations of AD pathogenesis alone [23]. Thus, several biological pathways have been proposed as leading mechanisms of AD and MCI [24, 25], and inflammation has emerged as a substantial driver of AD. There are studies that show increased levels of inflammatory markers in AD patients, as well as an association between AD risk genes and innate immune function [25–27]. The importance of inflammation in neurodegenerative processes of AD were observed for the first time 30 years ago, in a study that reported positive effects of chronic anti-inflammatory therapy on decreasing the incidence and progression of AD [28]. Epidemiological studies have also shown positive correlations between dementia and data on previous infection [29]. A number of confirmations followed, based on experimental studies on animal models [30] as well as clinical research [31], but also functional and structural changes in AD brain [32]. Eventually, based on the vast evidence [25–32], neuroinflammation is placed in the focus of the research in AD field, with promising potential to identify biomarkers of early phases of AD.

microRNAs (miRNAs) are small, endogenous, highly conserved, non-coding RNAs that regulate gene expression at the post-transcriptional level through RNA interference [33, 34]. miRNAs have been shown to be involved in fundamental cellular processes such as cell proliferation, differentiation, migration, and apoptosis [35]. A series of stud-

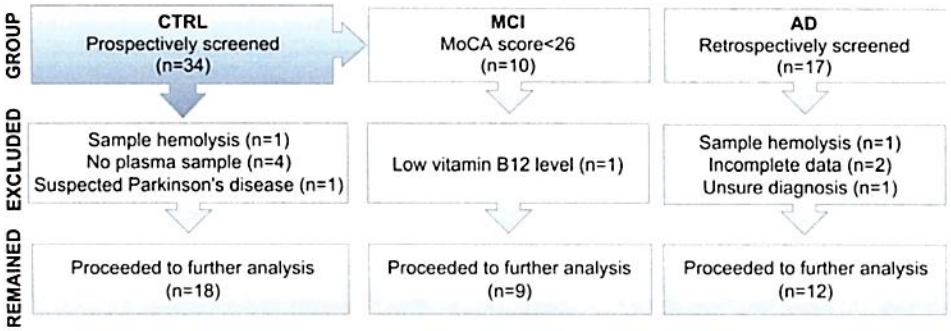

Fig. 1. Recruitment process. CTRL, healthy volunteers with normal cognitive function; MCI, healthy volunteers with subjectively normal cognitive function, but with mild cognitive impairment detected by neuropsychological screening; AD, participants diagnosed with AD.

ies demonstrated their implication in a variety of human brain dysfunctions involving neuroinflammation and oxidative stress [36]. Specifically, immune- and inflammation-related miRNAs are reported to have possibly crucial role in neuroinflammatory signaling pathways of AD [37,38].

Based on a detailed literature review, the analysis of the following circulatory miRNAs was conducted in the present study: miR-29a/b, miR-101, miR-125b, miR-146a, and miR-155. They have a role in the leading pathways of AD, such as: inflammation, oxidative stress, and innate immunity, and also in the specific processes involved in the formation of the abnormal protein deposits¾amyloid plaques and neurofibrillary tangles [39].

The presented study compared miRNA expression profiles in plasma of the three groups of patients: 1) those with AD (AD group), 2) those who subjectively have normal cognitive function, but objective tests show they have mild cognitive impairment (MCI group), and 3) those people who subjectively and objectively have normal cognitive function (CTRL group). In hope to identify future potential biomarkers for early stages of AD, we hypothesized that the expression levels of the selected circulatory miRNAs could correlate with the level of cognitive decline in participants.

MATERIALS AND METHODS

Ethical statement

The study protocol was approved by the Ethical Committee of the Clinical Center of Montenegro (No. 03/01-11417/1) and by the Committee for Medical Ethics and Bioethics of the Faculty of Medicine of the University of Montenegro (No. 3824/4). All the procedures were conducted in accordance with the Declaration of Helsinki.

Participants and group assignment

The present retrospective-prospective, multidisciplinary study enrolled 39 subjects, out of total 51 examined individuals (Fig. 1). They were divided into three groups: 18 healthy controls (CTRL), 9 patients with MCI, and 12 patients with previously diagnosed AD. Written informed consent to participate in the study was obtained from all participants or their legal representatives.

All the participants filled a questionnaire designed to standardize the process of the clinical interview and to obtain comparable demographic and clinical data (Table 1). Subsequently, they underwent the neurological and neuropsychological assessment, as well as peripheral blood sampling, for standard diagnostic and experimental laboratory analyses.

AD patients were recruited during their regular follow up appointments, at the Neurology Clinic of the Clinical Center of Montenegro. The other two groups of patients were volunteers recruited at the Faculty of Medicine.

For all participants excluding criteria were: presence of neurological disorder (other than AD, for AD group), psychiatric, systemic and poorly controlled chronic diseases, history of drug and alcohol abuse, and current acute illness. The Geriatric Depression Scale-15 (GDS-15) was performed to exclude depressive disorder. Those patients who scored 9 or more points on GDS-15 had major depression disorder and were excluded from the study [40]. In addition, in control subjects, neuropsychological screening test results [Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA)] below

26 were considered as excluding criteria. Nine participants who subjectively did not have cognitive impairment, but their MoCA score was lower than 26 formed a group with MCI. In these participants cognitive impairment was accidentally discovered.

A number of cases were excluded from the study, either because patients met exclusion criteria or plasma samples were inadequate (Fig. 1).

Clinical evaluation

Neurological examination

An interview according to the defined questionnaire, together with neurological examination, was conducted by a neurologist, at the Faculty of Medicine or at the Clinical Center of Montenegro. All the volunteers for the study, including those who denied neurological disorders during an interview, underwent detailed neurological examination, in order to thoroughly select participants for the study and identify exclusion criteria (Fig. 1).

Patients with AD were previously diagnosed at Clinical Center of Montenegro, according to the criteria of the National Institute of Aging and Alzheimer's Association (NIA-AA) [41]. At the time of the recruitment, they were neurologically re-evaluated for the purpose of research and identification of potential comorbidities defined as exclusion criteria. Results of the laboratory tests were used to confirm the presence of some of the participants' diseases, self-reported by the participant during the recruitment interview (Table 1).

Neuropsychological assessment

The neuropsychological examination of all participants was conducted by a doctor or a psychologist certified for neuropsychological assessment, which included: short assessment of SCD, MMSE, MoCA, and GDS-15. In AD patients, depression was previously excluded as a differential diagnosis, so the GDS-15 was not performed again.

Although the present study recruited people for the control group, who felt mentally and physically healthy, SCD was assessed through an open question as an additional check. Among the healthy volunteers, several participants unexpectedly had MoCA scores indicating they have an MCI, so they formed an MCI group. MoCA test score was used for the final selection of subjects for MCI group, since literature data consistently confirm its potential for improved detection of MCI and superiority compared to MMSE [42].

Laboratory examination

Biochemical laboratory analyses helped to identify conditions which are among excluding criteria (Fig. 1), or to check parameters of special interest for particular chronic disease of our study participants, which would exclude them from the study (e.g., HbA1 C>10). The following analyses were conducted for each study subject: complete blood cell count, glycemia, lipid status, liver enzymes, urea and creatinine, electrolyte status, thyroid function, folate, vitamin B12, and C-reactive protein as an inflammatory marker.

Table 1
Demographic and clinical features of the examinees

Variables	CTRL ($n=18$)	MCI ($n=9$)	AD ($n=12$)	P
Age (mean ± SD)	65.44 ± 8.12	70.33 ±8.46	70.92 ±7.34	0.1391
Median (range)	65.0 (55.0 – 77.0)	71.0 (55.0 – 82.0)	70.0 (59.0 – 85.0)	
Gender				0.6792
Male	11 (61.1%)	4 (44.4%)	6 (50%)	
Female	7 (38.9%)	5 (55.6%)	6 (50%)	
Years of education (mean ±SD)	13.72 ±2.52	11.44 ±3.97	11.25 ±3.05	0.0791
MoCA score (mean ±SD)	27.67 ±1.19	21.67 ±3.87	15.31 ±7.9	<0.0001***
Hypertension	8 (44.5%)	5 (55.5%)	8 (66.7%)	0.4857
Hyperlipidemia	7 (38.9%)	1 (11.1%)	5 (41.7%)	0.2691
Diabetes mellitus	3 (16.7%)	1 (11.1%)	5 (41.7%)	0.1756
Physical activity	12 (66.7%)	4 (44.5%)	7 (58.3%)	0.5413
History of smoking	8 (44.5%)	6 (66.7%)	4 (33.3%)	0.3106
Coffee consumption	12 (66.7%)	5 (55.6%)	3 (25%)	0.0785
Played music	3 (16.7%)	1 (11.1%)	2 (16.7%)	0.9212

SD, standard deviation; Physical activity, walking ≥ 30 min at least 5 days per week; History of smoking, current or former smokers; Coffee consumption, consumption of 3 or more cups daily; Played music, practicing of any kind of music (playing an instrument, singing, dancing), currently or previously in life.

Analysis of miRNA expression profiles

Sample processing and miRNA extraction

Ten milliliters of peripheral venous blood were collected from each participant into BD Vacutainer® Venous Blood Collection Tubes (cat. No. 367525) containing EDTA. The tubes were kept on ice and processed within 1 h from the blood collection. Plasma was separated from the whole blood by centrifugation at 1.900×g for 10 min at 4°C, followed by an additional centrifugation step at 3.000×g for 15 min at 4°C, to remove remaining cellular nucleic acids attached to cell debris. All samples were aliquoted in RNAse/DNAse-free tubes and stored immediately at –80°C until further analysis. MiRNA was isolated from plasma by using miRNeasy Serum/Plasma Advanced Kit (Qiagen, Hilden, Germany) according to the manufacturer's instructions. The miRNA concentration was determined using Qubit microRNA Assay Kit (Q32880, Invitrogen, Thermo Fisher Scientific) on a Qubit 3.0 fluorimeter (Q33216, Invitrogen, Thermo Fisher Scientific, USA).

Quantification of miRNAs by RT-PCR

Two µl miRNA from each sample was reversely transcribed to cDNA using TaqMan Advanced miRNA cDNA Synthesis kit (A28007, Applied Biosystems, USA) and analyzed with TaqMan Advanced microRNA Assays (A25576, Applied Biosystems, USA) for miR-29a/b, miR-101, miR-125b, miR-146a, and miR-155. qRT-PCR was run on an Applied Biosystems 7300 Real Time PCR system (Applied Biosystems, USA). The expression levels of target genes were normalized by using the mean expression levels of miR-361-5p gene, selected as the most stable internal control miRNA (between miR-186-5p, miR-1255a, and miR-361-5p) by the NormFinder algorhitm (Andersen CL, Jensen JL, Ørntoft TF). Normalization of real-time quantitative reverse transcription-PCR data: a model-based variance estimation approach to identify genes suited for normalization, applied to bladder and colon cancer data sets [43]. Expression of every target gene was calculated using the $2^{-\Delta\Delta Ct}$ method. Every sample was retrotranscribed twice and run in triplicate each time.

Statistical analysis

All statistical analyses were performed using GraphPad Prism 9.3.1 (GraphPad Software, San Diego, CA, USA) and the statistical software R. The results were considered statistically significant when $p < 0.05$. Continuous variables were analyzed with the *t*-test or one-way ANOVA, whereas categorical variables were analyzed with the χ^2 test or Fisher's exact test. Results of all continuous variables were first tested for normality of distribution by D'Agostino-Pearson and Shapiro-Wilk tests. Associations between miRNA expression and clinical variables were explored using Mann–Whitney and Kruskal-Wallis tests, as appropriate. Pearson correlation coefficients were computed as well. Receiver operating characteristic (ROC) curve analysis was done to evaluate all the five selected miRNAs as potential prognostic biomarkers.

RESULTS

Demographic and clinical features of the study participants

A summary of the demographic and clinical characteristics of study participants is given in the Table 1. There was no significant difference in age among the groups. Male and female examinees were almost equally represented in the groups. Participants of all the study groups had on average similar level of education.

As expected, MoCA scores among the groups were significantly different, with the lower values in patients with AD and MCI, compared to subjects in the control group ($p < 0.0001$, Table 1).

Hypertension, hyperlipidemia, and diabetes mellitus were the most common diseases among the study participants, but their prevalence was not significantly different among the groups. Frequency of habits, like smoking, coffee consumption, regular physical activity, and hobbies related to music, was similar among the groups. None of the participants had history of significant alcohol consumption.

MCI subjects without SCD were accidentally discovered by neuropsychological examination

None of the healthy volunteers in the study reported SCD (Table 2). The percentages of the volunteers with normal cognitive performance and those who scored under 26 on neuropsychological screening tests are given in the Table 2. MoCA and MMSE results were in correlation ($r = 0.725$; $p < 0.01$), but MoCA proved to be more sensitive since CI would not be discovered in 22.2% of examinees if they were evaluated by MMSE only (Fig. 2). When compared,

Table 2
Cognitive performance of the healthy volunteers

Evaluated category	Percentage of the examinees
Subjective cognitive decline	0%
MMSE score	
26-30	88.9%
<26	11.1%
MoCA score	
26-30	66.7%
<26	33.3%

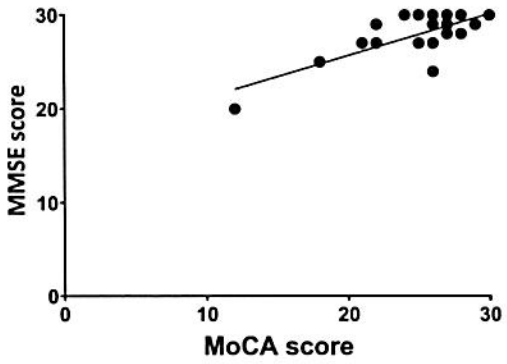

Fig. 2. Correlation of Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE) scores of the healthy volunteers.

MCI and control groups were not significantly different regarding the scores below 9 ($p = 0.36730$, data not shown).

Neurological examination of the control and MCI groups did not indicate presence of the central nervous system disease. The participants denied history of cerebrovascular or other neurological disease that could cause cognitive decline in the MCI group. Also, biochemical analyses of blood samples showed that none of the volunteers included in the study had thyroid dysfunction, B12 deficiency, severe anemia, acute or poorly controlled chronic condition that could cause cognitive decline.

miR-146a and miR-155 are upregulated in MCI subjects

Using the qRT-PCR method, in the CTRL, MCI, and AD groups, the expression level of the following circulatory miRNAs was determined: miR-29a/b, miR-101, miR-125b, miR-146a, and miR-155. Statistical analysis did not show any significant difference in the expression level of miR-29a/b, miR-101, and miR-125b among the examined groups ($p = 0.1512$, $p = 0.4374$, $p = 0.3020$ respectively, data not shown).

Circulatory miRNA-146a expression levels were found to be upregulated in MCI group, compared to both the CTRL ($p = 0.0121$) and AD group ($p = 0.0089$). Expression level of miR-146a in the control subjects, however, was not significantly different from those with AD ($p > 0.9999$) (Fig. 3A).

Similar pattern of expression among the groups was found for miR-155. Its expression level was significantly higher in participants with MCI, compared to the CTRL ($p = 0.0187$), but there was no difference in miR-155 levels between control and AD groups ($p = 0.2241$).

In order to have a more precise insight in sensitivity and specificity of these miRNAs in discrimination of healthy and diseased individuals and assess their potential to serve as a diagnostic test, ROC curve analysis was performed (Fig. 4A–C). For the miR-146a expression values of control and MCI groups, AUC was 0.8642 (95% MCI, 0.6852–1.0), with 77.8% sensitivity and 94.4% specificity (Fig. 4A), whereas for the data on miR-146a expression in participants with MCI and AD, AUC was 0.8519 (95% MCI, 0.6684-1.000) with 88.89% sensitivity and 83.33% specificity (Fig. 4B). When miR-155 expression level in the MCI and control groups was analyzed, AUC was 0.7654 (95% CI, 0.5474 to 0.9834), with 66.7% sensitivity and 88.9% specificity (Fig. 4C). Therefore, ROC curve analyses showed that both miR-146a and miR-155 had significant diagnostic value and could differentiate MCI from normal controls, and miR-146a could differentiate MCI from AD patients as well.

Moreover, although the expression of miR-155 was not different between MCI and AD group, the expression levels of miR-146a and miR-155 plotted together on a two-dimensional scatter plot illustrate a unique expression pattern of these selected inflamma-miRs that differentiates those with MCI from healthy individuals and from those with AD (Fig. 5).

miR-146a and miR-155 expression levels are unchanged during the course of manifested AD

Since miR-146a and miR-155 demonstrated the potential for detection of early cognitive impairment (Figs. 3 and 4), we wanted to test whether these miRNAs could also be upregulated earlier in the course of AD (Table 3). To that aim, expression values of miR-146a and miR-155 were compared between the patients diagnosed with AD less than one year before the moment of recruitment and those who had AD for one year or longer. The difference in the expres-

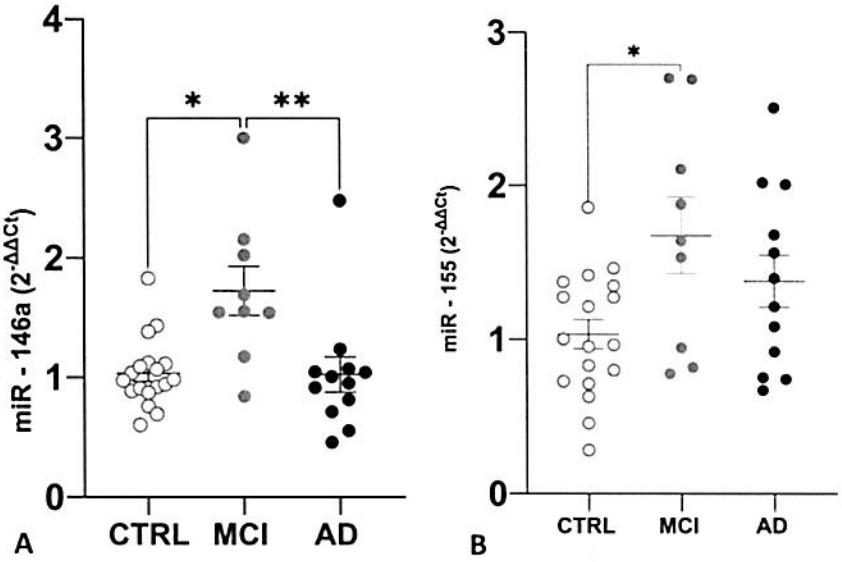

Fig. 3. A) Comparison of the circulatory miR-146a expression levels B) Comparison of the circulatory miR-155 expression levels. CTRL, control group; MCI, participants with mild cognitive impairment; AD, patients with Alzheimer's disease. *$p<0.05$, **$p<0.01$.

sion level was not statistically significant ($p=0.1120$, $p=0.8810$, respectively, data not shown). The correlation of miR-146a and miR-155 expression level with years of AD duration was not statistically significant ($p=0.7638$; $p=0.3027$, respectively, data not shown).

DISCUSSION

The present study enrolled patients with AD and volunteers without subjective cognitive decline, but interestingly, neuropsychological screening tests indicated that 33.3% of the apparently healthy subjects had MCI (Table 2). Neurological and laboratory findings could not explain their neuropsychological performance. However, in MCI group, the two circulatory miRNAs, miR-146a and miR-155, were upregulated compared to the control group of patients. The expression level of miR-146a was also significantly higher in MCI compared to AD group (Fig. 3). In patients with already diagnosed AD, miR-146a and miR-155 were not upregulated earlier in the course of the disease, compared to the later phases. Finally, ROC curve analyses suggested that these miRNAs could serve as non-invasive biomarkers of early cognitive impairment (Fig. 4).

Subjective cognitive decline is known as a phenomenon of self-experienced cognitive decline that may represent the first manifestation of AD, when objective impairment in cognition is still not present [11, 44]. Accidentally revealed MCI in healthy subjects who did not report SCD, and that we found in the present study (Table 2), has not been clinically recognized so far, to the best of our knowledge. Neuropsychological screening tests indicated that 33,3% of the apparently healthy subjects had MCI (Table 2), which could not be explained by neurological examination and laboratory findings. Many studies showed importance of SCD for early prediction of development of clinically manifested AD [11, 45, 46]. Moreover, neuroimaging techniques revealed distinctive brain alterations related to the symptoms of SCD [44, 47]. However, there are some critical points in the process of SCD evaluation that might be too subjective, affected by the individual cultural background and susceptible to the influence of various social factors and inter-personal relations at the moment of evaluation [12]. Our decision to use simple, open questions for SCD evaluation instead of structured questionnaires was in part driven by these facts. Results of neuropsychological screening tests used, MoCA and MMSE, were in correlation ($r=0.725$; $p<0.01$), but MoCA proved to be more sensitive, which is consistent with previously published data [42]. MCI would not have been discovered in 22.2% of the examinees, had they been evaluated by MMSE only (Fig. 2). Moreover, if the evaluation of SCD was not followed by an objective assessment, none of the participants with cognitive impairment would have been identified. Thus, our results certainly raise a question of reliability of subjective comprehension of cognitive functioning and emphasize significance

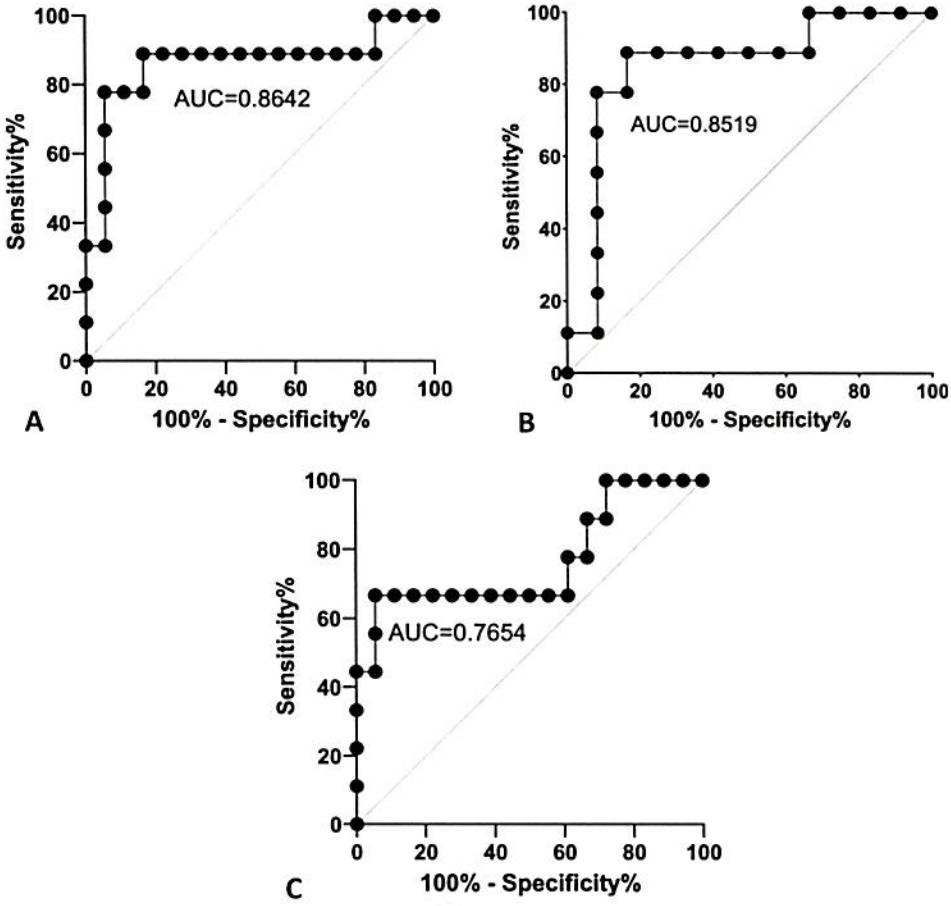

Fig. 4. Receiver operating characteristic (ROC) curve analysis of altered miRNAs. A) ROC for miR-146a in control and MCI groups; B) ROC for miR-146a in MCI and AD groups; C) ROC for miR-155 in control and MCI groups. CTRL, control group; MCI, participants with mild cognitive impairment; AD, patients with Alzheimer's disease.

of objective neuropsychological assessment. In order to rule out other causes of cognitive decline, history of other diseases, brain injury, and the list of medications were reviewed, and statistically significant difference in age among the groups was not found, which confirmed there was no significant difference among the groups (Table 1). The participants were also checked for vitamin B12 deficiency, thyroid dysfunction, anemia, and other acute or chronic conditions that could cause MCI. Finally, no significant variability in neurological examination or scale of depression was observed. However, it is worth noting that the extent of neurological evaluation in the presented study was limited to non-invasive and inexpensive tests and also, determined by the fact that AD patients have been retrospectively recruited.

The MCI group had significantly higher level of miR-146a and miR-155 expression, in comparison to the healthy control subjects (Fig. 3). Various studies conducted in humans or animal models and cell cultures, over the last ten years, unambiguously demonstrated involvement and significance of miR-146a and miR-155 in pathogenesis of AD [34, 48–52]. miRNA-146a was among the first miRNAs found to be highly expressed in AD brain, specifically in anatomical regions affected by the disease, but not in the other, control regions of the same brain [53]. Authors of the recent bioinformatics study created a miRNA-target interactions network constituted of 8 miRNAs and found that nodes in the network with the highest number of edges include miR-146 [54]. As for miR-155, its expression was found to be increased in AD rats, and its inhibition improved the impaired memory in this animal model [55].

When considering the continuum of clinical presentation of AD, it is of special interest to identify miRNA signature patterns of MCI stage, since it is estimated that up to 22% of individuals clinically

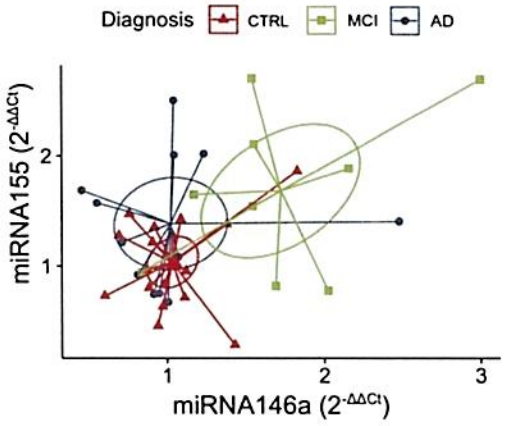

Fig. 5. Joint expression pattern of the selected inflammatory miRNAs differentiates the MCI group from the other two groups of participants. The graph represents a two-dimensional scatter plot of miRNA-146a and -155 expression levels. Each data point shows expression levels of miRNA-146a and -155 in plasma sample of one study participant, and it is labeled according to the associated diagnosis (CTRL, control; MCI, mild cognitive impairment; AD, Alzheimer's disease). The data clustering is illustrated by the superimposed star plot showing the mean value for a group in the center each cluster, which is surrounded by the 95% confidence area in the shape of the ellipse.

defined as MCI, progress to AD within one year [56]. Circulatory miR-146a is known to be significantly upregulated in patients with MCI who later develop AD, compared to those who do not convert to AD [48]. Also, higher miR-146 expression level was found in *APOE* E4 carriers, and it correlated with neuroimaging hallmarks of AD and increased CSF 42 amino acid amyloid-β ($A\beta_{42}$) concentration [48]. An interaction among MCI-associated genes and miR-155 was emphasized in the study by Strafella et al., which also found that miR-146 and miR-155 signaling pathways significantly interact in pathophysiological cascade of AD and other neurodegenerative diseases [57]. Taken together, these findings suggest that AD could be an underlying cause of the accidentally discovered mild cognitive impairment in volunteers in our study, who had increased expression of miRs-146a and -155, compared to the control group.

Closer understanding of miR-146a and -155 involvement in particular pathophysiological pathways of AD, further explains the significance of their increased expression level in MCI group. miR-146a, known for its importance in modulating the innate immune response and inflammatory events in brain cells [58], has been recently proposed as highly significant in neuroinflammatory mechanisms of AD [34, 48, 50, 57, 59, 60]. For example, in primary human neuronal-glial (HNG) cell co-cultures, miR-146a transcription was found to be induced by certain stress factors, such as the pro-inflammatory cytokine IL-1, known to be elevated in AD brain [58]. More recent research of inflammatory processes in AD also revealed significance of miR-155 in these pathways [33, 49, 57, 60]. This miRNA was shown to be early and strongly upregulated in 12-month triple transgenic mouse AD model [49], but also in Aβ-activated microglia and astrocytes, contributing to the production of inflammatory mediators such as IL-6 and IFN-β, inducing the decrease of activity of cytokine signaling suppressor (SOCS-1) [33]. Moreover, these studies revealed not only involvement of miR-146a and miR-155 in neuroinflammatory AD pathways, but also their interactive points in that cascade [57]. On the other hand, it is well established that neuroinflammation contributes to AD pathogenesis [25–32], and there is evidence that strongly suggests that it is initial and vital component in the AD pathophysiological cascade [61–65]. In an animal model, activation of microglia, which are key mediators of neuroinflammation among the innate immune cells, has been observed at the pre-plaque stage of AD [61]. Also, increased microglial activation has been detected in people with MCI, in the absence of amyloid tracer uptake [62, 63]. Genome-wide association studies found that mutations of microglial or innate immune genes, such as CD33, TREM2, and complement receptor type 1, are associated with an increased occurrence of AD in the population [64, 65], which also supports the neuroinflammatory concept as initiating in AD. All these data go in favor of hypothesis that an increase in expression levels of inflamma-miR-146 and -miR-155 in MCI subjects could be explained by their involvement in inflammatory pathways, characteristic for the early phase of AD pathophysiological events.

The presented results also showed that the expression levels of miR-146a and miR-155 were not statistically different between control and AD subjects and interestingly, miR-146a was still upregulated in MCI compared to AD group. More thorough insight in neuroinflammatory AD events and engagement of miR-146a and miR-155 in those pathways, could offer an explanation for such a result. Although essentially defensive, the immune response can cause harmful consequences if it is induced too strongly or for too long [32, 66]. Thus, at some time point, there is an activation of homeostatic mechanisms to limit destructive inflammatory events in AD [67, 68].

Table 3
Time frame of the disease course in AD patients

	Number of AD patients	Age at the beginning of the disease	Age at the moment of recruitment	Duration of the disease (mo)	miR-146a expression (mean)	miR-155 expression (mean)	*p*
AD diagnosed less than one year before the recruitment	5	76.4 ± 4.98	76.4 ± 4.98	3 ± 1.91	0.8478	1.349	0.1120
AD one year or longer	7	65 ± 5.47	67.4 ± 5.26	29 ± 16.81	1.150	1.404	0.5545

Data are presented as mean ± standard deviation.

Published data clearly indicate that miR-146a also has a role in suppression of pathological neuroinflammatory response in AD. Primarily induced by pro-inflammatory cytokines [58, 69, 70], miR-146a in turn downregulates proteins in overactive neuroinflammatory signaling pathways, contributing to their limitation [60]. Consequently, it is possible that this negative regulatory feedback mechanism ends with decreased expression of miR-146a. This consideration is supported by the research on primary neuronal cultures or neuroblastoma cell lines bearing Swedish mutation as AD cell models, which showed that miR-155 and miR-146a were highly expressed in microglia, responding to Aβ as a stress-related factor, with more prominent role of miR-155, which is found to be responsible for microglia polarization to pro-inflammatory M1 phenotype. Moreover, subsequent increase in inflammatory cytokines was followed by reduction of miR-146a expression, while miR-155 upregulation persisted [71]. Another study by the same authors [72] showed that presence of Aβ in different assembly states interacts with microglia leading to an inflammation cascade in young cells and that response is lost in aged cells, suggesting a differential response along the progression of AD. Temporal discrepancy of miR-146 and miR-155 expression during an inflammatory response was confirmed in animal model as well [73]. Increased expression of miR-155 induced overactive acute, but also chronic inflammation, even in a miR-146a-deficient mice.

These results are in line with our findings of miR-146a and miR-155 expression levels in clinical context. Significant miR-146a upregulation in MCI compared to control corresponds with its dominant role early in the disease process, through the initiation of inflammatory cascade and interaction with mediators of inflammation. Normalization back to control levels in AD group probably reflects suppression of miR-146a by homeostatic, anti-inflammatory mechanisms, characteristic for the chronic stage. On the other hand, miR-155 expression implicates its persistent activity, as a reflection of continuous, chronic, although self-limiting inflammation and continuous microglial engagement in that process.

However, other studies showed that disease progression in AD mouse models was followed by increased miR-146a expression in brain tissue [50], and also, it was observed in the same model *ex vivo*, that density of plaques and synaptic pathology were in correlation with miR-146a expression. Differences in methodological approach could be responsible for an opposite observation. Similarly, Lukiw et al. found that miR-146a levels measured in neocortex and limbic system increased, as the severity of AD advanced [58].

The number of participants is the limiting aspect of our study, thus, the research on the larger group is warranted in the future. Moreover, lack of the complete neurological evaluation in CTRL and MCI groups, that includes some invasive and expensive tests, might represent another limiting point of our study, but, at the same time, it has opened new directions for the future cohort study with the MCI group. Regular follow ups, screening of molecular and clinical inflammatory markers with complete neurological assessment at later time points, will potentially confirm AD as a cause of their cognitive impairment, as well as neuroinflammation as a key pathophysiological event. Also, cross-cultural validity of MoCA cutoff score and its adjustment for our region should be explored in the future. Eventually, results of our study imply that SCD evaluation through an open question might not always be reliable tool to indicate CI in elderly. Therefore, proposed structured evaluation form [11] should be considered as an assessment tool in the future studies.

Our results show that when analyzed together, the specific expression patterns of miR-146a and miR-155 are able to differentiate MCI group from the

control as well as from the AD group of participants (Fig. 5). AUC value of 0.8642 for miR-146a, with 77.8% sensitivity and 94.4% specificity (Fig. 4A), and AUC value of 0.7654 for miR-155, with 66.7% sensitivity and 88.9% specificity (Fig. 4C), clearly suggests their potential diagnostic significance for MCI detection. More research is needed to determine if these miRNAs could be used for detection of early AD stages in general population, as well as in patients with other comorbidities that were not included in this study.

Finally, our results on miRNA expression in patients with already diagnosed AD, which showed that miR-146a and miR-155 were not upregulated earlier in the course of the disease, compared to the later phases, additionally support their potential significance in detection of patients in MCI stage.

Conclusions

This study accidentally identified that a certain number of patients with cognitive decline in Montenegrin population remain undetected. SCD evaluation should be important and possibly critical aspect of the successful and timely detection of cognitive decline, but neuropsychological screening instruments should be routinely administered to elderly in Montenegro, even if the patient does not complain of problems related to cognitive functioning.

The upregulation of miR-146a and miR-155 could have utility in serving as a non-invasive, biofluid biomarker for the diagnosis of MCI due to AD and thus, potentially, also for monitoring of drug treatment efficacy and for making prognosis for the patients in early stages of AD.

Moreover, this study also identified the potential of neuropsychological screening instruments and molecular markers, which could together significantly improve our ability to diagnose AD in very early stage, and could possibly become routine non-invasive tools for detection of early AD.

Although determination of inflamma-miR-146a and -155 circulatory levels might represent a novel non-invasive biomarker for detection of an early stage of cognitive impairment due to AD, the research on the larger patient's cohort is warranted. Additionally altered miRNA and/or small non-coding RNA (sncRNA) levels may be uncovered and further improve the use of non-invasive, biofluid biomarkers for the diagnosis, drug treatment efficacy monitor and prognosis of early AD stages.

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BIOGRAFIJA

Isidora Rovčanin Dragović

Rođena je 1987. u Mojkovcu, gdje je završila osnovnu školu, a potom gimnaziju u Podgorici. Diplomirala je na Medicinskom fakultetu u Novom Sadu 2012. sa prosječnom ocjenom 9,23 i odbranila diplomski--istraživački rad sa ocjenom 10. Na Medicinskom fakultetu u Podgorici je 2013. upisala Doktorske studije i položila ispite sa prosječnom ocjenom 10.

Radila je kao ljekar Klinike za neurologiju Kliničkog centra Crne Gore, 2015/16. Specijalističke studije neurologije na Medicinskom fakultetu u Beogradu je upisala 2017. Sertifikovana je za neuropsihološku procjenu 2019. Zaposlena je na Katedri za fiziologiju Medicinskog fakulteta u Podgorici, gdje sprovodi praktičnu nastavu i naučno-istraživački rad.

U okviru Polaznog istraživanja je ispitivala uticaj magnezijuma na periferni nerv animalnog eksperimentalnog modela. Učestvovala je u međunarodnim projektima tokom kojih se edukovala iz oblasti biohemijskih i molekularno-bioloških tehnika, kao i za rad na ćelijskoj kulturi, u Institutu za istraživanje kancera i starenja u Nici i u Institutu za biomembrane i bioenergetiku u Bariju. U okviru nacionalnog projekta Medicinskog fakulteta, sprovela je translacionu neuronaučnu studiju za doktorsku disertaciju, kroz istraživanje uloga miRNK molekula u Alchajmerovoj bolesti. Samostalno je koncipirala još jedno istraživanje sa fokusom na Alchajmerovu bolest, čija je realizacija u toku.

Autor je i koautor 10 konferencijskih radova i 4 internacionalne žurnalske publikacije, kao i ad hoc recenzent u međunarodnim časopisima. Jedan je od urednika u vodećem međunarodnom časopisu - "Journal of Alzheimer's Disease".

Nagrade: diplome "Luča" za osnovno i srednje obrazovanje; najbolji istraživački rad na Internacionalnom kongresu studenata medicine u Novom Sadu, 2012; nagrada Ministarstva prosvjete Crne Gore za ostvareni prosjek 10 na Doktorskim studijama; najbolji prezentovan rad u oblasti Alchajmerove bolesti i demencija na Svjetskoj neurološkoj konferenciji o kontroverzama u neurologiji, 2022.

Govori engleski i njemački, služi se italijanskim i ruskim jezicima.

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povezivanje molekularnog znanja sa terapijom kancera, 2022 septembar; Cavtat, Hrvatska.

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10. Vučković Lj, Ždralević M, Raonić J, Radunović M, Popović N, Vukčević B, **Rovčanin Dragović I**, et al. Analiza nivoa ekspresije odabranih mikroRNK i njihova korelacija sa kliničkim i patološkim karakteristikama karcinoma kolona. Prvi kongres Sekcije za histologiju I embriologiju Srpskog ljekarskog društva, 2022 mart; Beograd, Srbija.
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12. **Rovčanin Dragović I**, et al. Influence of MgSO4 on survival time of isolated frog sciatic nerve in ex-vivo conditions. Četvrti kongres fizioloških nauka Srbije sa internacionalnim učešćem, 2018 septembar; Niš, Srbija. Knjiga sažetaka 2018; str. 127.
13. Popović N, Radulović A, **Rovčanin Dragović I**, et al. Impact of web-based learning management systems on education at the Faculty of Medicine in Podgorica, Montenegro. Dvadesetdruga konferencija informacionih tehnologija IT '17, 2017 mart; Žabljak, Crna Gora. Knjiga sažetaka 2017; str. 70-73.
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She was born in 1987 in Mojkovac where she finished elementary school and then gymnasium in Podgorica. She graduated from the Medical Faculty in Novi Sad in 2012 with an average grade of 9.23 and defended her graduate–research paper with a grade of 10. She enrolled in Doctoral studies in 2013 at Medical Faculty in Podgorica and passed the exams with an average grade of 10.

She worked as a doctor at the Neurology Clinic of Clinical Center of Montenegro in 2015/16. She enrolled in Specialistic Studies of Neurology at the Medical Faculty in Belgrade in 2017. She was certified for neuropsychological assessment in 2019. She works as a teaching and research assistant at the Physiology department of the Medical Faculty in Podgorica.

For the Initial research, she studied the effect of magnesium on the peripheral nerve of an animal model. She participated in international projects, during which she was educated in the field of molecular-biological techniques and for work on cell culture, at research institutes in France and Italy. As a part of the national project of the Medical Faculty, she conducted a translational neuroscientific study for her Doctoral Thesis, through research into the roles of miRNA molecules in Alzheimer's disease. She independently conceived another research with a focus on Alzheimer's disease, a realization of which is ongoing.

She is the author and co-author of ten conference and four international journal publications, as well as an ad hoc reviewer in international journals. She is one of the editors of the leading international journal – "Journal of Alzheimer's Disease"

Awards: "Luča" awards for primary and secondary education; the best research presentation at the International Congress of Medical Students in Novi Sad, 2012; Award of the Ministry of Education of Montenegro for achieving an average of 10 in Doctoral studies; the best

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and 5th Congress of the Croatian Physiological Society, 2022 September; Plitvice, Croatia.

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Izjavljujem

da je doktorska disertacija pod naslovom

Nova metoda za stratifikovanje rizika za obolijevanje od Alchajmerove bolesti kod pacijenata u Crnoj Gori

- rezultat sopstvenog istraživačkog rada,
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Potpis doktoranda

U Podgorici, _____

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Attachment 1.

Statement of authorship

Signed: Isidora Rovčanin Dragović, MD

Index number: 13/1

I state

that the Doctoral Dissertation, entitled:

A new method for stratification of the risk for Alzheimer's disease in patients in Montenegro

- is the result of my own research,
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Datum / Date 16.10.2017

Na osnovu člana 72 stav 2 Zakona o visokom obrazovanju („Službeni list Crne Gore" br. 44/14, 47/15,40/16,42/17) i člana 32 stav 1 .tačka 9 Statuta Univerziteta Crne Gore, Senat Univerziteta Crne Gore na sjednici održanoj 16.oktobra 2017.godine, donio je

O D L U K U
O IZBORU U ZVANJE

Dr Miodrag Radunović bira se u akademsko zvanje **redovni profesor za oblast Hirurgija- hepatobilijarna hirurgija na Medicinskom fakultetu,** na neodređeno vrijeme.

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2006 - Doktorske studije: Medicinski fakultet, Beograd; Tema: „Obim operativne traume kod klasične i minilaparotomijske holecistektomije"

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- 2016 predavac na predmetu Hirurgija na akademskom primijenjenom studijskom programu fizioterapije-Medicinski fakultet, Univerzitet CG

- 2016 Clan Medicinskog odbora Klinickog centra Crne Gore

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- 2015 -2016 Savjetnik predsjednika Vlade Crne Gore

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- 2012 - 2015 Predavač na akademskim postdiplomskim studijama, primijenjenim specijalističkim studijama na Ekonomskom fakultetu u Podgorici , smjer Ekonomija javnog sektora, Menadzment u zdravstvu

- 2012 Vanredni profesor, Medicinski fakultet u Podgorici,UCG, predmet: "Hirurgija – oblast: hepatobilijarna hirurgija" Medicinski fakultet, Stomatologija,

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- 1998-2004 Direktor JZU Opšta bolnica Berane

- 1997-2004 Predavač u Srednjoj medicinskoj školi Berane, predmet: „Hirurgija"

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- 1983-2003 Predavač u Srednjoj medicinskoj školi,"dr Branko Zogovic"Berane

- 1982-1984 Dom zdravlja Berane

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- 2019 novembar II Kongres UEHS sa medjunarodnim ucescem, Beograd

- 2019 mart STRUCNI SKUP na medjunarodnom nivou,UHFBiH, Tuzla ;Komplikacije u digestivnoj hirurgiji i transplantacije

- 18-20.09.2018 National meeting on health promotion in hospitalis, visit of prof.Hanne Tonnesen, WHO Expert, Podgorica

- 2018 april Naucna tribina,Calculosa zucne kese: Etiologija pristup dijagnostici i lijecenju,CANU,Podgorica

- 21-23.5.2015. Sedmi medjunarodni kongres "Ekologija, zdravlje, rad, sport" Banja Luka, BIH

- 8-11.10.2014 - First Congress of Physiotherapists of Montenegro with intrnational participation, Igalo, Montenegro

- 10.11.2014"Dijabetes u trudnoci, djetinjstvu i adolescenciji u Crnoj Gori" KME, IZJZ,Udruzenje endokrinologa CG,Udruzenje ginekologa i akusera CG, Udruzenje pedijatara CG

- 30.6 – 4.7.2014 - ECPD VI International Summer School of cardiovascular diseases: Risk Factor Control, Diagnostic and treatment of Cardiovascular diseases, Milocer, Montenegro

- 30.5 – 1.6.2014 - ECPD Internatioanl Specialist School: Modern arschievements in prevention, therapy and rehabilitation of addictive diseases, Kotor, Montenegro

- 23-27.5.2014 godine - ECPD International Summer School Menagement of Haelth -Institutions: Haelth Care Systems of South Eastern Europe at the Crossroads View tothe Future After a Decade of Reforms, Milocer, Montenegro

- 2013 - Clan Uredjivackog savjeta Medical Journal of Montenegro,

- 26-28.06.2013 - Ministarska konferencija o univerzalnoj zdravstvenoj pokrivenosti, Istanbul, Turska

- 2013 oktobar - XIV Kongres drustva ljekara CG sa medjunarodnim ucescem, Becici, Budva, Crna Gora

- 17.9.2013 - EACCME-Postgraduate course-How to cure and maintain a haelthy stomach, Milocer, Montenegro

- 2012 jun -29-th Meeting of the South- eastern Europe Health Network;First Regional Conference on Organ Donation and Transplantation >Heart to the Region<-Beating towards self Sufficiency, Zagreb, Croatia.

- 2012 novembar - I Regionalni kongres "Suporativna terapija onkoloskih bolesnika" Sarajevo, BiH

- 15-17.11.2012 - 6th Meeting of International Endohernia Society organizied by Serbian Hernia Society, Belgrade

- 25-29.6.2012 - ECPD III International SUmmer School: Prevention and treatmentof Cardiovascular diseases, Milocer

- 23.4.2012 -"Rano otkrivanje raka - gdje smo danas"IzJZ , KME,Podgorica

- 2011 - I Globalna ministartska konferencija o zdravim stilovima života i kontroli nezaraznih bolesti, Moskva

- 19-20.11.2010 - 4th Intensive Balkan Telemedicine and E- Health Seminar, Podgorica

- 2008-2009. - Član Upravnog odbora Univerziteta Crne Gore

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UDŽBENIK I MONOGRAFIJA

1. Pajović B. **Radunović M.** Hirurgija za studente visoke medicinske škole. Medicinski fakultet UCG. Podgorica. ISBN 9789940-657-03-1-2014.1-477

2. Ratković-Mugoša M. **Radunović M.** Pajović B. Radojević N. Jovanović M. Najčešće unutrašnje bolesti i biohemijski parametri. Podgorica: Medicinski fakultet UCG. 2013.193 str. ISBN 978-9940-657-01-7

3.Pajović B. **Radunović M.** Ašanin B. Gluščević S. Hirurška propedevtika za studente Visoke medicinske škole. Medicinski fakultet - Univerzitet Crne Gore. 2010.

4. Pajović B. i sar. Brodska medicina i medicinska briga. Udžbenik za studente Pomorskog fakulteta u Kotoru. **Radunović M.** (3 poglavlja) a) Povrede i njihovo zbrinjavanje b) Naglo nastale bolesti c) Medicinski značaj masovnih nesreća na moru – izdavač Univerzitet Crne Gore Medicinski fakultet 2012.

5. **Radunović Miodrag.** Radunović Miroslav: Anatomske odlike i vrednosti aproksimacione teorije u izboru metode zbrinjavanja defekata ingunalnog kanala: IJZCG Podgorica. 2006. COBISS CG-ID 10912528.2006. CIP 616-007.43-089.11

6. Radunović M. **Radunović M.** Citohistološke i morfometrijske karakteristike kardiomiocita nastale imobilizacionim stresom pacova. Izdavač Institut za javno zdravlje Crne Gore. Podgorica. 2012. ISBN 978- 86-8557-31-6 COBISS.CG-ID 20394768

RUKOVODILAC PROJEKTNOG TIMA :

1.New methods for risk stratification for progression of cancer and Alzheimer's disease in patients in Montenegro (DEMONSTRATE)"- naučno-istraživački projekat finansiran od strane Ministarstva nauke na period od 2 godine (april 2019 - mart 2021).

2.Project on the Strengthening Capacity for appropriate use of antibiotic prophylaxis in surgery (BCA-2018. Moh Mne and WHO)

3.Project Haelth promotion in Hospital 2018-2020. WHO

4.Morfološka i klinička istraživanja bioloških mehanizama vaskularnog remodelovanja naslednih i stečenih bolesti krvnih sudova UCG –Medicinski fakultet. 2012-2015

Univerzitet Crne Gore
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Na osnovu člana 72 stav 2 Zakona o visokom obrazovanju („Službeni list Crne Gore" br 44/14, 47/15, 40/16, 42/17, 71/17, 55/18, 3/19, 17/19, 47/19 i 72/19) i člana 32 stav 1 tačka 9 Statuta Univerziteta Crne Gore, Senat Univerziteta Crne Gore na sjednici održanoj 16.09.2020. godine, donio je

O D L U K U
O IZBORU U ZVANJE

Dr Nataša Popović bira se u akademsko zvanje vanredni profesor Univerziteta Crne Gore za **oblast Funkcionalna grupa bazičnih medicinskih predmeta,** na Medicinskom fakultetu Univerziteta Crne Gore, na period od pet godina.

SENAT UNIVERZITETA CRNE GORE
PREDSJEDNIK

Prof. dr Danilo Nikolić, rektor

CV MENTORA

Doc. dr Nataša Popović je šef Katedre za medicinsku fiziologiju na Medicinskom fakultetu Univerziteta Crne Gore i specijalista porodične medicine sa medicinskom licencom u državi Teksas u Sjedinjenim Američkim Državama, i u Crnoj Gori.

Njen glavni istraživački interes usmeren je na fiziologiju starijeg životnog doba kao i na patogenezu hroničnih bolesti koje se javljaju u ovom životnom periodu. Njeno naučno istraživanje u prethodnih par godina je posvećeno razvoju metoda za neinvazivnu kvantifikaciju efekata faktora rizika za razvoj kardiovaskularnih bolesti na remodeliranje mikrovaskulature ljudskog tela.

Dr. Nataša Popović je 1998. godine stekla zvanje doktora medicine u Srbiji na Medicinskom fakultetu u Novom Sadu, a školovanje je nastavila u Sjedinjenim Američkim Državama, na Texas A&M Univerzitetu (College Station, Texas), gdje je magistrirala iz oblasti ljudske ishrane 2003. godine. Zatim, 2008. godine je doktorirala iz oblasti medicinskih nauka na katedri za Medicinsku fiziologiju Texas A&M Health Science Centra (College Station, Texas), gde je nastavila da radi kao postdoktorski istraživački saradnik do 2009. godine. Za to vreme je u laboratoriji za vaskularnu biologiju proučavala životinjske modele hipertenzije, remodeliranje krvnih sudova koje se javlja udruženo sa kardiovaskularnim faktorima rizika i ovladala je primenom molekularno bioloških tehnika kao što su RT PCR i microarray. Pored toga, dr Popović je završila specijalizaciju iz porodične medicine u Texas A&M Health Science Centru 2012. godine. U periodu od 2012. do 2015. godine radila je kao lekar u urgentnom centru u bolnici St. Joseph (College Station, Texas). Od 2015. godine, dr Nataša Popović radi u zvanju docenta na Medicinskom fakultetu u Podgorici kao šef Katedre za medicinsku fiziologiju.

Izabrani projekti:

1. **Rukovodilac partnerskog projektnog tima** sa Medicinskog fakulteta Univerziteta Crne Gore na **H2020-SC1-BHC-2018** projektu. "Retinal and Cognitive Dysfunction in Type 2 Diabetes: Unraveling the Common Pathways and Identification of Patients" at Risk of Dementia "- RECOGNISED. Ovaj projekat predstavlja produkat kolaboracije između 20 vodećih naučno-istraživačkih institucija iz Evrope. Projekat počinje sa realizacijom u januaru 2020.
2. **Rukovodilac projekta/** potencijalni mentor na projektu: Neinvazivne metode u procjeni rizika za razvoj koronarne arterijske bolesti (NEMEKOR). Student doktroskih studija, dr Mirko Lipovac i dr Nataša Popović su zajedno podneli prijavu na **Konkurs za dodelu doktorskih stipendija** koji je raspisan od strane Ministarstva nauke Crne Gore u aprilu 2019. godine. Dr Lipovac je na ovom konkursu osvojio stipendiju kojom će finansirati naučno istraživanje u periodu od 36 meseci sa početkom 01.11.2019. godine.
3. **Ključni ekspert na nacionalnom naučno-istraživačkom projektu**: Nove metode za stratifikaciju rizika za progresiju kancera i Alchajmerove bolesti kod pacijenata u Crnoj Gori (DEMONSTRATE). Projekat je počeo 01.04.2019. i trajaće do 31.03.2021.
4. Član tima na **bilateralnom projektu između Ministarstva nauke Crne Gore i The National Research Council of Italy**. Naziv projekta je: Disfunkcija mitohondrija u rastu kancera, rezistentnosti na lijekove i hemioterapijom-indukovanoj neuropatiji. Ovaj projekat je trajao od 01.01.2017 do 31.12.2018.

Objavljeni naučni radovi:

1. Regional Patterns in Retinal Microvascular Network Geometry in Health and Disease. **Popovic N**, Vujosevic S, Popovic T. Sci Rep. 2019 Nov 8;9(1):16340. doi: 10.1038/s41598-019-52659-8
2. Fractal characterization of retinal microvascular network morphology during diabetic retinopathy progression. **Popovic N**, Lipovac M, Radunovic M, Ugarte J, Isusquiza E, Beristain A, Moreno R, Aranjuelo N, Popovic T. Microcirculation. 2019 Jan 19:e12531. doi: 10.1111/micc.12531
3. Manually segmented vascular networks from images of retina with proliferative diabetic and hypertensive retinopathy. **Popovic N**, Radunovic M, Badnjar J, Popovic T. Data Brief. 2018 Mar 15;18:470-473. doi: 10.1016/j.dib.2018.03.041.
4. Fractal dimension and lacunarity analysis of retinal microvascular morphology in hypertension and diabetes. **Popovic N**, Radunovic M, Badnjar J, Popovic T. Microvasc Res. 2018 Jul;118:36-43 doi: 10 1016/j mvr 2018 02.006.
5. A Moodle-based blended learning solution for physiology education in Montenegro: a case study **Popovic N**, Popovic T, Rovcanin Dragovic I, Cmiljanic O. Adv Physiol Educ. 2018 Mar 1;42(1):111-117. doi: 10 1152/advan.00155.2017
6. The pterygopalatine fossa: morphometric CT study with clinical implications. Vuksanovic-Bozaric A, Vukcevic B, Abramovic M, Vukcevic N, **Popovic N**, Radunovic M. Surg Radiol Anat. 2019 Feb;41(2):161-168. doi: 10.1007/s00276-018-2136-8.
7. Morphometric characteristics of the optic canal and the optic nerve. Radunovic M, Vukcevic B, Radojevic N, Vukcevic N, **Popovic N**, Vuksanovic-Bozaric A. Folia Morphol (Warsz). 2018 Aug 14. doi: 10.5603/FM.a2018.0065.
8. Complications of Laparoscopic Cholecystectomy: Our Experience from a Retrospective Analysis Radunovic M, Lazovic R, **Popovic N**, Magdelinic M, Bulajic M, Radunovic L, Vukovic M, Radunovic M. Open Access Maced J Med Sci. 2016 Dec 15;4(4):641-646. doi: 10.3889/oamjms.2016.128.
9. Regional changes in elastic fiber organization and transforming growth factor β signaling in aortas from a mouse model of marfan syndrome. Howell DW, **Popovic N**, Metz RP, Wilson E. Cell Tissue Res 2014 Dec;358(3):807-19 doi. 10 1007/s00441-014-1993-7
10. Time course of carotid artery growth and remodeling in response to altered pulsatility. Eberth JF, **Popovic N**, Gresham VC, Wilson E, Humphrey JD. Am J Physiol Heart Circ Physiol. 2010 Dec;299(6):H1875-83. doi: 10.1152/ajpheart 00872.2009.
11. Transforming growth factor-beta signaling in hypertensive remodeling of porcine aorta. **Popovic N**, Bridenbaugh EA, Neiger JD, Hu JJ, Vannucci M, Mo Q, Trzeciakowski J, Miller MW, Fossum TW, Humphrey JD, Wilson E. Am J Physiol Heart Circ Physiol. 2009 Dec;297(6):H2044-53. doi: 10.1152/ajpheart.01015.2008.
12. Importance of pulsatility in hypertensive carotid artery growth and remodeling. Eberth JF, Gresham VC, Reddy AK, **Popovic N**, Wilson E, Humphrey JD. J Hypertens. 2009 Oct;27(10):2010-21. doi: 10.1097/HJH.0b013e32832e8dc8.
13. Aberrant crypt foci and semiparametric modeling of correlated binary data. Apanasovich TV, Ruppert D, Lupton JR, **Popovic N**, Turner ND, Chapkin RS, Carroll RJ. Biometrics. 2008 Jun;64(2):490-500.
14. Tissue-specific attenuation of endogenous DNA I-compounds in rats by carcinogen azoxymethane: possible role of dietary fish oil in colon cancer prevention. Zhou GD, **Popovic N**,

Lupton JR, Turner ND, Chapkin RS, Donnelly KC. Cancer Epidemiol Biomarkers Prev. 2005 May;14(5):1230-5.

15. Testing for spatial correlation in nonstationary binary data, with application to aberrant crypt foci in colon carcinogenesis. Apanasovich TV, Sheather S, Lupton JR, **Popovic N**, Turner ND, Chapkin RS, Braby LA, Carroll RJ Biometrics 2003 Dec;59(4):752-61.

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Број: 08-3699
Датум, 19.12.2013 г.

Ref:
Date,

Na osnovu člana 75 stav 2 Zakona o visokom obrazovanju (Sl.list RCG, br. 60/03 i Sl.list CG, br. 45/10 i 47/11) i člana 18 stav 1 tačka 3 Statuta Univerziteta Crne Gore, Senat Univerziteta Crne Gore, na sjednici održanoj 19.12.2013. godine, donio je

O D L U K U
O IZBORU U ZVANJE

Dr sci med. MILICA MARTINOVIĆ bira se u akademsko zvanje **redovni profesor** Univerziteta Crne Gore za predmet: Patološka fiziologija i labaratorijska medicina, na Medicinskom fakultetu.

REKTOR
Prof. dr Predrag Miranović

Prof.dr Milica Martinović- prijava za komentorstvo za izradu doktorske disertacije dr Miloša Luklća

BIOGRAFIJA

Rodjena 29.X 1960. g. U Nikšiću , Crna Gora. Osnovnu školu i gimnaziju završila u Nikšiću. Diplomirala na Medicinskom fakultetu Univerziteta u Beogradu 1983.g. Specijalizaciju iz pedijatrije završila 1992.g, položivši sa odličnom ocjenom specijalistički ispit, na Institutu za zdravstvenu zaštitu majke i deteta Medicinskog fakulteta Univerziteta u Beogradu. Magistarski rad pod nazivom „ Komparativna studija etiopatogenetskih i kliničkih parametara bronhijalne astme sa efektima terapije u kontinentalnom i priobalnom dijelu Crne Gore" odbranila 1997.g. na Medicinskom fakultetu Univerziteta u Nišu, Srbija. Zvanje doktora medicinskih nauka stekla na Medicinskom fakultetu Univerziteta u Nišu, odbranivši doktorsku disertaciju pod nazivom „ Uloga i značaj primjene inhalacionih glikokortikoida u prevenciji dječije astme".

Od 1999. Zaposlena na Medicinskom fakultetu Univerziteta Crne Gore, na predmetu Patološka fiziologija i laboratorijska medicina. U zvanje docenta izabrana 2003.g., vanredni profesor 2008., a u zvanje redovni profesor 2013.g.

IZVODI IZ BIBLIOGRAFIJE

REDOVI U ČASOPISIMA SA SCI LISTE

1. Jaksic M, Martinovic M, Gligorovic-Barhanovic N, Vujacic A, Djurovic D, Nedovic-Vukovic M. Association between inflammation, oxidative stress, vitamin D, copper and zinc with pre-obesity and obesity in school children from the city of Podgorica, Montenegro, Journal of Pediatric Endocrinology and Metabolism, 2019,https://doi.org/10.1515/jpem-2019-0086
2. Duborija Kovacevic N, Martinovic M, Belojevic G, Lausevic D, Asanin B. Maternal Education, Health Profession and Cigarette Smoking are Decisive Factors for Self-Medication in Children by Parents, Acta Pharm.2019. http://doi.org/10.2478/acph-2020-0018
3. Milica Martinovic, Goran Belojevic, Marina Jaksic, Nebojsa Kavaric, Aleksandra Klisic CARDIOMETABOLIC RISK AMONG MONTENEGRIN URBAN CHILDREN IN RELATION TO OVERWEIGHT AND OBESITY Acta clinica Croatica,prihvaćen za objavljivanje
4. Aleksandra Klisić, Nebojša Kavarić, Bojko Bjelaković, Ivan Soldatović, Milica Martinović, Jelena Kotur-Stevuljević Povezanost retinol-vezujućeg proteina 4 i kardiovaskularnog rizika posredovana je obimom struka kod pretilih/debelih adolescentica Acta clinica Croatica, Vol.56. No.1. (str.98-98), mart 2017.
5. M. Martinovic , G. Belojevic , G.W. Evans, N. Kavaric, B. Asanin ,S. Pantovic, M. Jaksic,J. Boljevic Hypertension and correlates among Montenegrin schoolchildrend a cross-sectional study, Public Health 147 (2017),15-19, SCI, IF 1.566

6. Aleksandra Klisić, Jelena Kotur Stevuljević,Nebojša Kavarić, Milica Martinović, Marija Matić, The association between follicle stimulating hormone and glutation peroxidase activity is dependent on abdominal obesity in postmenopausal women, Eating and Weight Disorders - Studies on Anorexia, Bulimia and Obesity, pp 1–9, 2016, available on http://link.springer.com/article/10.1007%2Fs40519-016-0325-1
7. Marina Jaksic , Milica Martinovic , Goran Belojevic, Nebojsa Kavaric , Bogdan Asanin, Mira Samardzic, Snezana Pantovic, Jelena Boljevic; The Prevalence of and Contributing Factors to Overweight and Obesity Among the Schoolchildren of Podgorica, Montenegro, Srpski arhiv za celokupno lekarstvo, 2017., Vol 1-2, pp 20-25
8. Mira Samardzic, Milica Martinovic, Mirjana Nedovic-Vukovic,Milena Popovic-Samardzic, Recent incidence of type 1 diabetes mellitus in Montenegro: shift toward a younger age at onset of the disease, Acta Clin Croat 2016; 55:63-68
9. Milica Martinovic, Goran Belojevic, Gary W. Evans, Dragan Lausevic, Bogdan Asanin at al.Prevalence of and contributing factors for overweight and obesity among Montenegrin schoolchildren, Eur J Public Health (2015) 25 (5): 833-839
10. Pantović Snežana, Božović Dragica,Nikolić Goran,Martinović Milica, Mitrović Predrag, Radulović Lenka,Isaković Aleksandra, Marković Ivanka „ Markers of inflammmation and antioxidative enzyme activities in restenosis following percutaneous coronary intervention " , Journal of the Serbian Chemical Society 2015, 80 (2), 143
11. Martinović M, Belojević G, Evans GW, et al. Blood pressure among rural Montenegrin children in relation to poverty and gender. Eur J Pub Health 2014;24(3):385-9.
12. Martinović M. News In the pathophysiology ofasthma, Vojnosanitetski pregled, 2013, Vol VI. Str. 84-87
13. Duborija-Kovačević N., Martinović M.Evaluation of farmacotherapy of obstructive airway diseases in the Montenegrin outpatient care: comparison with two Scandinavian countries,Multidisciplinary Respiratory Medicine 2012,7:123

Radovi objavljeni u časopisima koji se ne nalaze u medjunarodnim bazama podataka

14. Milica Martinović, Sigurnosni profil inhalacionih kortikosteroida (beclomethason dipropionat)primijenjenih u konvencionalnim i u visokim dozama u prevenciji dječje astme, ACTA MEDIKA MEDIANAE, ISSNYU 0365-4478, Vol.47, No.1,2008.

15. Martinović M, Pejakov Lj. Child asthma and environmental factors in Montenegro. (Originalstudija) Jurnal Medical Brasovean, Brasov 2010; Vol VI, (3):73-75. ISSN 1841-0782.

16. Pejakov Lj, Martinović M. Perioperative outcome: genetics, environment or both. (Editorial) Jurnal Medical Brasovean, Brasov 2010; Vol VI, (3):4-7. ISSN 1841-0782.

17. Martinović M., Inhaled corticosterolds: the role in the prevention of asthma, pathophysiological and clinical aspects, Jurnal Medical Brasovean, Brashov, 2012, ISSN 1841-0782.nr.2-2012

PROJEKTI

1. Rukovodilac crnogorskog nacionalnog naučno-istraživačkog projekta " Istraživanje siromaštva i gojaznosti kod školske djece u Crnoj Gori- klinički, patofiziološki, biohemijski i preventivni aspekti", 2013-2015.

2. Koordinator za Medicinski fakultet u Podgorici CEEPUS projekta: » Developing a network for monitoring the Impact of environmental and nutritional factors on fertility and neonatal health«, Network Coordinator assoc.prof Marius Moga, Transilvania University of Brashov, Romania, 2007- 2013

3. Rukovodilac crnogorskog tima u bilateralnom crnogorsko-hrvatskom projektu : „ Komparativna studija o uticaju siromaštva na pothranjenost i gojaznost, dijetetske navike i životni stil kod skolske djece Podgorice i Osijeka" Član istraživačkog tima

4. CRNOGORSKO-SRPSKI BILATERALNI PROJEKAT: „Značaj praćenja odnosa mokraćnwe kisjeline i oksidativnog stresa u definisanju kardiovaskularnog rizika metabolički zdrave i metabolički bolesne djece sa viškom tjelesne mase" (The importance of monitoring the interrelation between uris acid and oxidative stress in defining cardiovascular risk at metabolically healthy and sick children with excess body weight"), član istraživačkog tima

5. Competency based Curriculum Reform in Nursing and Caring in Western Balkan Universities 544169-TEMPUS-1-2013-1-BE-TEMPUS-JPCR, rukovodilac prof.dr Bogdan Ašanin, član istraživačkog tima

6. Član istraživačkog tima u projektu Ministarstva nauke CG- „Balneološki efekti peloida, mineralne vode, ljekovitog i aromatičnog bilja na inflamatorni odgovor kod reumatoidnih i kardiovaskularnih bolesti", rukovodilac doc.dr Snežana Pantović

7. Član istraživačkog tima u projektu Ministarstva nauke CG- „Procjena jodnog statusa, razvoj i standardizacija preventivnog programa u Crnoj Gori", rukovodilac prof.dr Mira Samardžić

Na osnovu člana 32 stav 1 tačka 14 Statuta Univerziteta Crne Gore, u vezi sa članom 29 Pravila doktorskih studija, Senat Univerziteta Crne Gore, u postupku razmatranja prijedloga Vijeća Medicinskog fakulteta br. 4027 od 16.11.2016. godine, na sjednici održanoj 12.01.2017. godine, donio je sljedeću

O D L U K U

I

Dr Milica Martinović, redovni profesor Medicinskog fakulteta Univerziteta Crne Gore, imenuje se za komentora pri izradi doktorske disertacije kandidatkinji Isidori Rovčanin, pored mentora doc. dr Nataše Popović imenovane Odlukom Senata br. 03-2154/2 od 27.102.106. godine.

II

Odluka stupa na snagu danom donošenja.

Broj: 03- 3390/6-2016
Podgorica, 12.01.2017. godine

PREDSJEDNIK SENATA

Prof. Radmila Vojvodić, rektor

Na osnovu člana 32 stav 1 tačka 14 Statuta Univerziteta Crne Gore, u vezi sa članom 29 Pravila doktorskih studija, Senat Univerziteta Crne Gore, u postupku razmatranja prijedloga Vijeća Medicinskog fakulteta br. 2191 od 11.07.2016. godine, na sjednici održanoj 27.10.2016. godine donio je sljedeću

O D L U K U

I

Dr Nataša Popović, docent Medicinskog fakulteta Univerziteta Crne Gore, imenuje se za **mentora** za izradu doktorske disertacije studentu doktorskih studija, **dr med. Isidori Rovčanin.**

II

Senat upućuje preporuku Vijeću Medicinskog fakulteta da predloži i komentora, zbog činjenice da predloženi mentor ima zvanje docent i da je prvi put mentor za izradu doktorske disertacije.

III

Odluka stupa na snagu danom donošenja.

Broj: 03-2154/2
Podgorica, 27.10.2016. godine

PREDSJEDNIK SENATA

Prof. Radmila Vojvodić, rektor

УНИВЕРЗИТЕТ У БЕОГРАДУ

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СЕНАТ УНИВЕРЗИТЕТА
У БЕОГРАДУ

Београд, 22.6.2016. године
06-01 Број: 61202-2264/3-16
ТК

На основу чл. 65. ст. 2. Закона о високом образовању ("Службени гласник РС", број 76/05, 100/07-аутентично тумачење, 97/08, 44/10 и 93/12), чл. 42. ст. 1. тач. 23. и чл. 43. ст. 4. Статута Универзитета у Београду ("Гласник Универзитета у Београду", број 186/15-пречишћени текст), чл. 25. ст. 1. и ст. 2. тач. 1. Правилника о начину и поступку стицања звања и заснивања радног односа наставника Универзитета у Београду ("Гласник Универзитета у Београду", број 142/08, 150/09 и 160/11) и Критеријума за стицање звања наставника на Универзитету у Београду ("Гласник Универзитета у Београду", број 183/15-пречишћени текст), а на предлог Изборног већа Медицинског факултета, број: 6586/2 од 6.4.2016. године и мишљења Већа научних области медицинских наука, број: 61202-2264/2-16 од 17.5.2016. године, Сенат Универзитета, на седници одржаној 22.6.2016. године, донео је

О Д Л У К У

БИРА СЕ др Елка Стефанова у звање редовног професора на Универзитету у Београду-Медицински факултет, за ужу научну област Неурологија.

О б р а з л о ж е њ е

Медицински факултет је дана 28.10.2015. године у листу „Послови" објавио конкурс за избор у звање редовног професора, за ужу научну област Неурологија, због потреба Факултета.

Извештај Комисије за припрему извештаја о пријављеним кандидатима стављен је на увид јавности дана 2.3.2016. године преко сајта и огласне табле Факултета.

На основу предлога Комисије за припрему извештаја о пријављеним кандидатима, Изборно веће Медицинског факултета, на седници одржаној дана 6.4.2016. године, донело је одлуку о утврђивању предлога да се кандидат др Елка Стефанова изабере у звање редовног професора.

Медицински факултет је дана 25.4.2016. године доставио Универзитету комплетан захтев за избор у звање на прописаним обрасцима.

Универзитет је комплетну документацију коју је доставио Факултет ставио на web страницу Универзитета дана 10.5.2016. године.

Веће научних области медицинских наука, на седници одржаној дана 17.5.2016. године дало је мишљење да се др Елка Стефанова може изабрати у звање редовног професора.

Сенат Универзитета, на седници одржаној дана 22.6.2016. године разматрао је захтев Медицинског факултета и утврдио да кандидат испуњава услове прописане чл. 64. и 65. Закона о високом образовању, чланом 125. Статута Универзитета у Београду, као и услове прописане Критеријумима за стицање звања наставника на Универзитету у Београду, па је донета одлука као у изреци.

ПРЕДСЕДНИК СЕНАТА

Академик Владимир Бумбаширевић

Доставити:
- Факултету (2)
- архиви Универзитета
- сектору 06

A. OSNOVNI BIOGRAFSKI PODACI

- Ime, srednje ime i prezime: Elka (Dimitar) Stefanova
- Datum i mesto rodjenja: 21. Avgust .1959; Bitolj
- Ustanova gde je zaposlen: Medicinski Fakultet, Univerzitet u Beogradu
- Zvanje/radno mesto: Redovni profesor
- Naučna, odnosno umetnička oblast: Neurologija

B. STRUČNA BIOGRAFIJA, DIPLOME I ZVANJA

Osnovne studije:

- Naziv ustanove: Medicinski Fakultet, Univerzitet u Beogradu
- Prosečna ocena: 9.68
- Mesto i godina završetka: 1984 godina, Beograd

Magisterijum:

- Naziv ustanove: Medicinski Fakultet, Univerzitet u Beogradu
- Mesto i godina završetka: Beograd, 1989 godina
- Naslov: «Neuropsihološki poremecaji u dece sa kongenitalnim hipotireoidizmom»
- Mentor: prof dr D. Vranješević
- Članovi komisije: Prof. dr D. Vranješević, Prof. dr V. Išpanović, Prof. dr S. Radmanović
- Uža naučna, odnosno umetnička oblast: Neurologija

Doktorat:

- Naziv ustanove: Medicinski Fakultet, Univerzitet u Beogradu
- Mesto i godina odbrane: Beograd, 1995 godina
- Naslov disertacije: "Proceduralno i Deklarativno pamćenje u Parkinsonovoj bolesti i u amnestičkom sindromu" .
- Mentor: prof. Dr Vladimir Kostić
- Članovi komisije: Prof. dr V. Kostić, Prof. dr G. Ocić, Prof. dr Lj. Rakić
- Uža naučna, odnosno umetnička oblast: Neurologija

Specijalizacija: 1992 -Specijalistički ispit iz Neuropsihijatrije (Medicinski fakultet, Univerzitet u Beogradu) položila je sa najvišom ocenom.

Dosadašnj izbori u nastavna i naučna zvanja:

- Od 1997 do 2004. dr Elka Stefanova je bila u zvanju asistenta na Katedri za Neurologiju, Medicinskog Fakulteta, Univerziteta u Beogradu (izbor i reizbor)
- Od 2004 godine ima zvanje docenta na katedri za Neurologiju, Medicinskog Fakulteta, Univerziteta u Beogradu
- 2009 godine je ponovo reizbrana u zvanje docenta na katedri za Neurologiju.
- 2010 je izabrana u zvanje vandrednog profesora na katedri za Neurologiju.
- 2015 reizbrana u zvanje vandrednog profesora na katedri za Neurologiju
- 2016 izbarna u zvanje redovnog profesora profesora na katedri za Neurologiju
-

Poglavlja u Internacionalnim monografijama (peer reviewed)

1. Stefanova E, Kostić VS, Ocić G, Ziropadja Lj. Cognitive deficits in Alzheimer's disease, Parkinson's disease, and Huntington's chorea. In: Fisher A, Hanin I, Yoshida M (eds) Progress in Alzheimer's and Parkinson's disease. Plenum Press, New York, 1998, pp 377-383.
2. Nordberg A, Stefanova E, Shori-Dareh T, Wall A, Langstrom B. Neuroimaging and cholinesterase inhibition. In Giacobini E (ed) Butyrylcholinesterase: Its Function and Inhibitors, 2003, pp 91-101.
3. Kostic V, Stefanova E., Dragašević N, Potrebić S. Diagnosis and treatment of depression in Parkinson's disease. In Bedard M-A, Agid Y, Chouinard S, Fahn S, Korczyn AD, Lesperance P. Mental and behavioral dysfunction in movement disorders, Humana Pres Inc., Totowa NJ.2003, pp 351-368

Poglavlja u monografijama od nacionalnog značaja:

1. Ocić G., Stefanova E., Pavlović D., Nenadović M.: Neuropsihološki model istra-ivanja kognitivnih poremećaja izazvanih hroničnim alkoholiizmom; U Nenadović M. (ur.): Narkomanija i alkoholizam; Medicinski fakultet u Beogradu; Beograd, 1995; 139-145.

2. Ocić G., Stefanova E., Pavlović D.: Terapija demencije. u Kostić V., Sokic D.(ur.): Novine u lecenju neuroloških obolenja. Beograd 1997; 37-49.
3. Stefanova E., Kostić V. Genetika demencije. (urednici Kostić V. Apostolski S. Romac S. Genetika u Neurologiji.Beograd 1999, pp 148-158.
4. Kostic V. Dragašević N., Čuljković B., Stojković O., Svetel M., Vukosavić S. Stefanova E., Romac S. Poliglutaminske bolesti. Lekcije dekade mozga. Lekcije dekada mozga Beograd 2001, (urednici Kostić V. Apostolski S.) str 41-83.
5. Zarkovic M. Stefanova E. MELAS. Klinicki seminar 374, Instituta za endokrinologiju i bolesti metabolizma, Beograd 2000.
6. Stefanova E.: Osvrt na klasifikaciju vaskulnih kognitivnih poremećaja. U Raičević Ranko i Vladimir Kostić, Klasifikacije i kriterijumi u neurologiji. Beograd 2006.
7. Stefanova E i Vladimir Kostić.Farmakoekonomija demencije.U Prostran Milica, Ranka Samardić. Timotijević Ivana, Durić Dušan. Farmakoekonomija u psihijatriji. Beograd 2006.
8. Stefanova E.: Inhibitori holinesteraze i memantin u lečenju demencije .U: Tončev Gordana urednik. Novine u terapiji neuroloških bolesti, Udruženje neurologa Srbije, Kragujevac, 2007, 95-114.
9. Stefanova E. Dijagnostički i klinički kriterijumi u proceni opšte radne sposobnosti telesnog oštećenja u demenciji. U Jelena Mihajlev Simpozijum sa medjunarodnim učešćem o veštačenju u neurologiji, Novi Sad, 20-22.09. 2007
10. Stefanova E. Demencija u Parkinsonovoj bolesti. Crnogorski medicinski pregled 2008; 95-100
11. Stefanova E. i sar. Nacionalni vodič dobre kliničke prakse u dijagnostikovanju i lečenju Alchajmerove bolesti ISBN 978-86-83607-82-2. Izdavač Ministrastvo Zdravlja Republike Srbije, 2013

Predavanja po pozivu na međunarodnim skupovima

1. Thessaloniki, November 20-23, 2003: 1st congress on Brain and behaviour International society on Brain and behaviour: round table. Movement disorders and the mind: Depression in Parkinson disease.
2. Szeged, September22: Joint symposium of Serbian and hungarian neurologists : Neuropsycholoical investigation in Parkinson disease.
3. "Sinapsa" : 6.10. 2007, Ljubljana: Executive deficits in neurological diseases
4. Basal ganglia Slovenia: 19.06. 2008 Ljubljana: MCI in Parkinson's disease .
5. ALS symposium Fagane: 19 sept 2008 Ljubljana: Executive dysfunction in ALS
6. „Sinapsa" 26 septembar 2009 Ljubljana: Memory in a Clinical Setting: Bedside Testing,
7. IV simpozijum o cerebrovaskulnim bolestima, Oktobar 26-28 , 2010. „Internacionalni Sastanka Trends in Neurosonology" Vaskulni faktori rizika i neurodegenerativne bolesti.
8. „Sinapsa „ septembar 2011.Ljubljana . „CSF biomarkers in Alzheimer disease, Parkinson disease, and atypical parkinsonism"
9. Brac- Brac Academy of Neurology: Differential diagnosis of dementia 20.05. 2011
10. Pula 2011. 51. INPC-u 15-18 juna 2011 Fronto-Temporal dementia and Atypical parkinsonismus -soft boundaries
11. Riga 2011: Seventh International Congress on Vascular Dementia 2011, October 20-23, 2011. Lecture : Vascular risk factors in Alzheimer disease.
12. XIV Nacionalni kongres Udruženja Psihiajatara Srbije i III kongres Udruženja psihijatara Istočne Evrope i Balkana, Psihijatrioski dani suplemntum 2012: Nadomak biološke dijagnoze Alzheimerove bolesti i drugih srodnih bolesti _ Biomarkeri iz cerebropsinalne tečnosti.
13. SIMPOZIJUM SA MEĐUNARODNIM UČEŠĆEM Drugi memorijalni simpozijum „Petar Arežina" ISTRAŽIVANJA U NEUROLOŠKOJ REHABILITACIJI 09. Novembar 2012, Beograd, Svečana sala Srpske akademija nauka i umetnosti: Cognition and Gait.
14. Dubrovnik 2013: Adratic Forum-24-28 aprila 2013: Lecture: Young Onset dementia-dfferential diagnosis.
15. IX/X kongres Neurologa Srbije sa medjunarodnim učešćem. . Novembar 14-16, 2013, Beograd „Amiotrofička lateralna skleroza i frontotemporalna demencija - funkcionalna konvergencija."
16. IX/X kongres Neurologa Srbije sa medjunarodnim učešćem. Novembar 14-16, 2013, Beograd. „Frontotemporalna demencija- klinički izazov „
17. Belgrade: MDS WINTER SCHOOL 2014: 28Feb-2.March 2014. "Psychogenic movement disorders"
18. Nica 2014 : 10th International Congress on Non-Motor Dysfunctions in Parkinson's Disease and Related Disorders, Nice, December 4-7, 2014 Lecture: Anxiety in Parkinson disease.
19. First International Ohrid meeting, Septembar 26-27, 2014 „Parkinson disease and dementia"
20. Beograd Peti kongres lekara opšte medicine sa medjunarodnim učešćem, Oktobar 2-5, 2014„ Alchajmerova bolest u svetlu novih saznanja".
21. Dubrovnik 2015-«Dubrovnic Academy of Neurology» 2015 Fronto-Temporal Dementia-evolving concept.

22. Sofija Bulgarin Medical Academy 2016 Spectrum of cognitive disorders in Parkinsonism -from MCI to DLB-
23. Sofija : Bulgarian Society on Dementia „Depression in PD" 2017 April 8th
24. KME Wilsonova bolest 2017
25. Kongres Neurologa 2017 Beograd Novembar "Demencija/parkinsonizam sindromi"
26. SANU 2017 „200 godina od monografije Jamesa Parkinsona „Spektar kognitivnih poremećaja u Parkinsonovoj bolesti"
27. Škola Mladih Neurologa: 12-13 oktobar 2018: "Demencija"
28. Adriatic forum Monopoli 2018: Genetics in Early Onset Dementia (EoD)" -report from Belgrade Memory clinic".
29. Kongres Neurologa 2019 Vrnjačka banja Amiotrofička lateralna skleroza -kognitivni i bihejvioralni ispadi-
30. Kongres Neurologa Novembar 27-29 2019 Vrnjačka banja "Biomarkeri za Alzheimerovu bolest" -da li je ovo veliki zaokret?-
31. Kongres Neurologa 2019 Novembar 27-29 Vrnjačka banja: Karotidna stenoza uzrokuje kognitivno oštećenje?
32. Kongres Neurologa 2019 Novembar 27-29: Lečenje nemotornih poremećaja u Parkinsonovoj bolesti
33. Kongres Neurologa 2019 Novembar 27-29: Edukativni kurs Kognitivni domeni: Pamćenje
34. Adriatic 2019 Budva 2019 "Biomarkers for Alzheimer disease –Is it a turning point"
35. FTD European Workshop Tricase (Lecce) Italy, February 6-7th : „Dementia in Serbia „

c) Organizovanje naučnih sastanaka i simpozijuma

1. Član Organizacionog odbora kongresa neurologa Srbije u Kragujevcu 2008.
2. KME Dijagnoza i terapija demencija, mart 2004
3. KME Da li smo na putu optimalnog lečenja multiple skleroze, maj 2004
4. KME Vaskulne demencije, decembar 2005
5. KME Vaskulna demencija , april 2006
6. Akademija medicinskih nauka srpskog lekarskog društva naučni skup: Demencije: Alzheiemerova bolest nova saznanja, 18. januar 2010.
7. KME „Savremeni pristup u laboratorijskoj dijagnostici demencija" 26 mart 2010.
8. Srpsko lekarsko društvo sekcija za Patološku Anatomiju, Alzheiemerova bolest-savremeni koncept. 23.April.2010.
9. KME:"Amiotrofična lateralna skleroza i frontotemporalna demencija- funkcionalna konvergencija"-28. Mart 2013. Beograd:
10. Stremljenja i novine u Medicini –decembar 2013. "Kognitivno-bihejvioralni aspekti u neurodegenerativnim oboljenjima: luksuz ili nužnost?
11. Belgrade: MDS WINTER SCHOOL 2014: 28 Feb-2.March 2014.
12. Ljubljana oktobar 2015 regionalno predsedništvo za organizaciju International Conference of Vascular Dementia (ICVD 2015)
13. SANU 2017 200 godina od monografije Jamesa Parkinsona „Spektar kognitivnih poremećaja u Parkinsonovoj bolesti"
14. KME Wilsonova bolest 2017
15. Škola Mladih Neurologa: 12-13 oktobar 2018: "Demencija"
18. Update in Parkinson' s disease SANU 2018
19. Update on Dementia SANU 2019

d) Rukovodjenje ili učešće na projektima

1. Molekularna dijagnostika naslednih neuroloških bolesti (br. 1988; rukovodilac projekta Prof Dr V.S. Kostić)
2. Genetička osnova neurodegenerativnih bolesti. Projekat Akademije nauka, rukovodilac projekta Prof. Dr V.S. Kostić
3. Istraživanje kliničkih i genetičkih korelacija motornih i nemotornih ispoljavanja bolesti nevoljnih pokreta (broj projekta 145057; rukovodilac projekta Prof Dr V.S. Kostić).
4. Degenerativne bolesti mozga, (rukovodilac projekta profesor V.S Kostić, broj projekta 175090).
5. "Strategies to prevent cognitive decline in non-demented subjects 2017-2021 Alz. Assoc. Grant AACSFD-17-533520 mentor projekta

Spisak Literature 2010-2020

1. Filippi M, Basaia S, Sarasso E, et al. Longitudinal brain connectivity changes and clinical evolution in Parkinson's disease [published online ahead of print, 2020 May 14]. *Mol Psychiatry*. 2020;10.1038/s41380-020-0770-0. doi:10.1038/s41380-020-0770-0 - (M21a)
2. Kresojević N, Mandić-Stojmenović G, Dobričić V, et al. Very Late-Onset Niemann Pick Type C Disease: Example of Progressive Supranuclear Palsy Look-Alike Disorder. *Mov Disord Clin Pract*. 2020;7(2):211-214. Published 2020 Jan 22. doi:10.1002/mdc3.12892
3. Stefanova E, Dubljević O, Herbert C, et al. Anticipatory feelings: Neural correlates and linguistic markers. Neurosci Biobehav Rev. 2020;113:308-324. doi:10.1016/j.neubiorev.2020.02.015 (M21a)
4. Salak-Djokic Biljana Stojkovic Tanja Mandic-Stojmenovic Gorana B Stefanova Elka DA profile of dementia patients in a Serbian sample - experience from the center for dementia and memory disorders (Article) VOJNOSANITETSKI PREGLED, (2020), vol. 77 br. 3, str. 271-281 (M23)
5. Marković V, Stanković I, Petrović I, et al. Dynamics of impulsive-compulsive behaviors in early Parkinson's disease: a prospective study. *J Neurol*. 2020;267(4):1127-1136. doi:10.1007/s00415-019-09692-4 (M21)
6. Mehrabian S, Schwarzkopf L, Auer S, et al. Dementia care in the Danube Region. A multi-national expert survey. Neuropsychiatr Dis Treat. 2019;15:2503-2511. Published 2019 Aug 29. doi:10.2147/NDT.S161615- (M22)
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9. Stojkovic T, Stefanova E, Soldatovic I, et al. Exploring the relationship between motor impairment, vascular burden and cognition in Parkinson's disease. J Neurol. 2018;265(6):1320-1327. doi:10.1007/s00415-018-8838-3 (M21)
10. Canu E, Agosta F, Mandic-Stojmenovic G, et al. Multiparametric MRI to distinguish early onset Alzheimer's disease and behavioural variant of frontotemporal dementia. Neuroimage Clin. 2017;15:428-438. Published 2017 May 25. doi:10.1016/j.nicl.2017.05.018 (M21)
11. Marjanović IV, Selak-Djokić B, Perić S, et al. Comparison of the clinical and cognitive features of genetically positive ALS patients from the largest tertiary center in Serbia. J Neurol. 2017;264(6):1091-1098. doi:10.1007/s00415-017-8495-y 3 (M21)
12. Bosco P, Redolfi A, Bocchetta M, et al. The impact of automated hippocampal volumetry on diagnostic confidence in patients with suspected Alzheimer's disease: A European Alzheimer's Disease Consortium study. Alzheimers Dement. 2017;13(9):1013-1023. doi:10.1016/j.jalz.2017.01.019 (M21a)
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14. Galantucci S, Agosta F, Stefanova E, et al. Structural Brain Connectome and Cognitive Impairment in Parkinson Disease. Radiology. 2017;283(2):515-525. doi:10.1148/radiol.2016160274 (M21a)
15. Macesic M, Lalic NM, Kostic VS, et al. Impaired Insulin Sensitivity and Secretion in Patients with Alzheimer's Disease: The Relationship with Other Atherosclerosis Risk Factors. Curr Vasc Pharmacol. 2017;15(2):158-166. doi:10.2174/1570161114666160905170644 (M22)
16. Kramberger MG, Auestad B, Garcia-Ptacek S, et al. Long-Term Cognitive Decline in Dementia with Lewy Bodies in a Large Multicenter, International Cohort. J Alzheimers Dis. 2017;57(3):787-795. doi:10.3233/JAD-161109 (M21)
17. Popovac A, Stancic I, Despotovic N, Nikolic S, Stefanova ED Milasin JM, Difference in Apolipoprotein E Genotype Distribution Between Dentate and Edentulous Elderly Patients with Alzheimer Disease (Article) GENETIKA-BELGRADE, (2016), vol. 48 br. 2, str. 699-706(M23)
18. Stojkovic T, Stefanova E, Pekmezovic T, Peric S, Stevic Z. Executive dysfunction and survival in patients with amyotrophic lateral sclerosis: Preliminary report from a Serbian centre for motor neuron disease. Amyotroph Lateral Scler Frontotemporal Degener. 2016;17(7-8):543-547. doi:10.1080/21678421.2016.1211148 (M22)

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22. Canu E, Agosta F, Sarasso E, et al. Brain structural and functional connectivity in Parkinson's disease with freezing of gait. Hum Brain Mapp. 2015;36(12):5064-5078. doi:10.1002/hbm.22994 (M21a) (M21)
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24. Peric SZ, Mandic-Stojmenovic G. **Stefanova ED** Savic-Pavicevic DLj Pesovic J, Ilic V, Dobricic VS Basta I Z. Lavrnic D. S Rakocevic-Stojanovic VM.Frontostriatal dysexecutive syndrome: a core cognitive feature of myotonic dystrophy type 2 . Journal of Neurology 2015. vol. 262 br. 1, str. 142-148 **(M21 Impact Factor 3.745)**
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26. **Stefanova E**, Žiropadja L, Stojković T, Stanković I, Tomić A, Ječmenica-Lukić M, Petrović I, Kostić V. Mild Cognitive Impairment in Early Parkinson's Disease Using the Movement Disorder Society Task Force Criteria: Cross-Sectional Study in Hoehn and Yahr Stage 1. Dement Geriatr Cogn Disord. 2015;40(3-4):199-209. **(M21; impact factor 3.24)**
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28. Mandic-Stojmenovic G, **Stefanova E**, Dobricic V, Novakovic I, Stojkovic T, Jesic A, Kostic V. Screening for C9orf72 Expansion Mutation in Serbian Patients with Early-Onset Dementia. Dement Geriatr Cogn Disord. 2015 Sep 25;40(5-6):358-365. **(M21; Impact factor 3.24)**
29. Rakocevic-Stojanovic V, Peric S, Madzarevic R, Dobricic V, Ralic V, Ilic V, Basta I, Nikolic A, **Stefanova E**. Significant impact of behavioral and cognitive impairment on quality of life in patients with myotonic dystrophy type 1. Clin Neurol Neurosurg. 2014. **(M23 , impact Factor 1.468)**
30. **Stefanova E**, Ječmenica Lukić M, Ziropadja L, Marković V, Stojković T, Tomić A, Dragašević Mišković N, Kostić V. Attentional set-shifting in Parkinson's disease patients with freezing of gait-acquisition and discrimination set learning deficits at the background? J Int Neuropsychol Soc. 2014 Oct;20(9):929-36 **(M21, Impact Factor 3.617)**
31. Peric S, Mandic-Stojmenovic G, Markovic I, **Stefanova E**, Ilic V, Parojcic A, Misirlic-Dencic S, Ostojic M, Rakocevic-Stojanovic V, Kostic V. Cerebrospinal fluid biomarkers of neurodegeneration in patients with juvenile and classic myotonic dystrophy type 1. Eur J Neurol. 2014 Feb;21(2):231-7 **(M21, impact Factor 3.852)**
32. Agosta F, Canu E, **Stefanova ED**, Sarro L, Tomic AD, Spica V, Comi G, Kostic VS Filippi M. Mild cognitive impairment in Parkinson's disease is associated with a distributed pattern of brain white matter damag. Human Brain Mapping, 2014, vol. 35 br. 5, str. 1921-1929 **(M21, Impact Factor 6.956)**
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Prevod sa engleskog jezika

Curriculum Vitae

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Adresa	Institut za biomembrane, bioenergetiku i molekularnu biotehnologiju (IBIOM) – Bari – CNR, Via Amendola 122/D 70126 Bari, Italija	
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RADNO ISKUSTVO

1994. do danas Istraživačica CNR-a (Nacionalni istraživački savjet Italije) pri Institutu za biomembrane, bioenergetiku i molekularnu biotehnologiju (IBIOM) – Bari – CNR

2020. Članica Naučnog komiteta Forsajt zdravstvene grupacije (*Foresight Health group*) u segmentu CNR (Nacionalni istraživački savjet Italije) S&T (naučno-tehnološki) Forsajt projekta, sa ciljem promocije inicijativa za pomoć definisanju naučnih strategija pogodnih za adekvatno rješavanje glavnih društvenih izazova, kao što su: energija, hrana, zdravlje, voda.

2020. Članica Naučnog komiteta za drugi master nivo u „Integrisanom medicinskom i prehrambenom menadžmentu u cilju prevencije i liječenja kancera" – Odsjek medicinskih nauka – Univerzitet u Kataniji.

2018. Članica Akademskog odbora za doktorske studije iz oblasti funkcionalne i primijenjene genomike i proteomike – Univerzitet u Bariju.

2017. Pune profesorske kvalifikacije za molekularnu biologiju - Nacionalna naučna kvalifikacija (ASN)

2015. do 2017. Gostujuća profesorica za molekularnu biologiju (Bačelor iz medicine i hirurgije – Univerzitet u Bariju)

2008. do 2015. Gostujuća profesorica u Laboratoriji za molekularnu biologiju i bioinformatiku (Fakultet za biotehnologiju – Univerzitet u Bariju)

2000. Gostujuća istraživačica u Laboratoriji za kampanju istraživanja kancera prof. ser Dejvid-a Lejn-a (*Prof. Sir David Lane*), Odsjek za hirurgiju i molekularnu onkologiju – Univerzitet u Dandiju (*Dundee*), Škotska

1999. do danas Mentorka za doktorske radove, stipendije, obuke i studente

1993-1994. Stipendija CNR (Nacionalni istraživački savjet Italije)

1992-1993. Stipendija Evropske organizacije za molekularnu bilogiju (EMBO) na Institutu za istraživanje biologije tumora – Laboratorija dr. Karwan, Bečki univerzitet (Austrija)

OBRAZOVANJE I OBUKE

2009. Sekvenciranje sledeće generacije (*NGS*) 454 GS FLX titanijumske serije (*Roche*) praktična obuka

2001. Obuka na platformi za protočnu citometriju *Becton Dickinson FACSCaliburTM*

1997. Master iz kliničke i laboratorijske onkologije: pomjeranje granica u biotehnologiji i terapiji neoplazija

1993. Doktorat iz oblasti biohemije i molekularne biologije

1988. Stručni državni ispit iz biologije

1986. Diploma iz oblasti bioloških nauka (*summa cum laude*) na Univerzitetu u Bariju

NAUČNA DJELATNOST

Odgovorno lice za sledeće naučne projekte:

- Istraživačka jedinica 1 Projekat PIR01_00017 CNRBiOmics „Jačanje platforme za visokopropusnu produkciju –OMIK / OMIC podataka" (Nacionalni bioinformatički istraživački centar za „-OMIK" nauke) (2019-2021)

- Istraživačka jedinica za projekat *Interomics* (2017-2018): „Istraživanje transfera između različitih vrsta: efekat mikroRNK egzogenih biljaka na ekspresiju humanih gena u vezi sa bolestima izazvanim procesom starenja"

- Istraživačka jedinica za projekat *Progetto n.57*, prot.AOO_044 datiran 14/12/2009-0015366-0008015, Onkološka bio-banka u Pulji (BioBOP) – „Mreža za korišćenje kontrolisanih onkoloških tkiva okarakterisanih razvojem novih dijagnostičkih pristupa, farmakoloških i biomedicinskih" (2009-2013)

- *Caripuglia* projekat 2011-2012 „Razvoj nove terapije tumora zasnovane na biopeptidima sposobnim za obnavaljanje aktivnosti p53 onko-supresora"

- Istraživačka jedinica za istraživačke projekte od nacionalnog interesa PRIN 2007

Participacija u drugim naučnim projektima:

- Istraživački projekti od nacionalnog interesa PRIN (1999-2000) Bioinformatička i genomička istraživanja

- Izrada planova za jačanje naučno-tehnološke mreže klastera Ministarstva za univerzitetska, naučna i tehnološka istraživanja Italije *MURST Cluster C03* (2000-2003)

- Pružanje izuzetnog doprinosa, istaknutog u ministarskom dekretu D.M. br. 1105 od 09.10.2002. Ministarstva nauke i prosvete Italije (MIUR). Nacionalni operativni program „Naučno istraživanje, tehnološki razvoj, visoko obrazovanje" 2000/2006.

- Nacionalni istraživački program *PNR* 2001-2003 (Fond za investicije u istraživanje *FIRB* čl.8) ministarski dekret D.M.199, Strateški program: *Post-genom*, odobrenje 31-063933; Istraživanje i razvoj novih bioinformatičkih i biotehnoloških instrumenata za analizu genetske i proteinske profilne ekspresije kancera i za identifikaciju bioloških markera za rânu dijagnostiku kolorektalnih i bubrežnih neoplazija, te neoplazija usne šupljine" (2006-2009)

- Fond za investicije u istraživanje *FIRB* 2003 čl. 8; upravni dekret D.D. 2187 od 12.12.2003; Protokol: RBLA039M-LIBI: Međunarodna bio-informatička laboratorija (2005-2010)

- Projekat FAR LAB. B. 8 „Privatno-javna laboratorija za bioinformatiku primijenjenu u genomici" DM19410 (2007-2010)

- Istraživački projekat Italijanske fondacije za multiplu sklerozu (FISM) „Visokopropusno ispitivanje infektivnih agenata povezanih sa multiplom sklerozom putem nepristrasnog dubinskog sekvenciranja kDNK" (2008-2009)

- PON01_01297 VIRTUALB – Napredni sistemi biomedicinske mehatronike za dijagnostiku i medicinsku terapiju zasnovani na virtuelnoj i proširenoj stvarnosti, mikroelektronici i visokopropusnim robotičkim laboratorijama.

- PON01_02589 „Razvoj multipleks tehnoloških platformi za molekularnu dijagnostiku, portabl i automatizovanu, zasnovanu na instrumentalnoj logici „laboratorija na čipu", koja dozvoljava multi-parametarske aplikacije infektivnog polja". Skraćenica: „MikroMapa".

- Bilateralni italijansko-crnogorski projekat „Mitohondrijalna disfunkcija rasta kancera, otpornost na medikamente i neuropatija izazvana hemoterapijom", Institut za biomembrane, bioenergetiku i molekularnu biotehnologiju IBIOM - Univerzitet Crne Gore, Fakultet za medicinu i hirurgiju u Podgorici (2017-2018).

- Projekat POR Pulja FESR-FSE 20142020 Aktivnost 1.6. Najava „Ino-mreža / Innonetwork", kôd 1JLZKD0, dekret A.D. b.124 od 16.10.2017: „OMICS4FOOD „Poboljšanje procesa proizvodnje svježe hrane proizvedene od brašna, pomoću OMIK tehnologija i kompleksnih informacija, elaboriranih u informacionom sistemu, dizajniranom i razvijenom u *Cloud* okruženju" (2018-2020).

- Projekat Ministarstva nauke Crne Gore „Nove metode za stratifikaciju rizika progresije kancera i Alchajmerove bolesti kod pacijenata u Crnoj Gori (DEMONSTRATE)" (1-04-2019 – 31-03-2021)

- Istraživački projekat „IDF SHARID – Inovativni uređaji za upravljanje rizikom od dijabetesa", identifikacioni kôd ARS01_01270 u okviru industrijskog istraživanja i eksperimentalnog razvoja u 12 oblasti za specijalizaciju, identifikovanih u Nacionalnom istraživačkom programu PNR 2015-2020.

- Projekat industrijskog istraživanja i eksperimentalnog razvoja u 12 oblasti za specijalizaciju, identifikovanih u Nacionalnom istraživačkom programu PNR 2015-2020. „BIOMIS" – Uspostavljanje biobanke za intestinalne mikrobiote i humanu pljuvačku: od dizbioze do simbioze„ identifikacioni kôd ARS01_01220 (od 01.07.2018. do 30.06.2021).

- Projekat HORIZON 2020 – H2020-INFRAEOSC-2018-2020, INFRAEOSC-04-2018, RIA, broj predloga: SEP-210489595, skraćenica „EOSC-LIFE", broj 824087 – naslov projekta „Obezbjeđivanje otvorenog prostora za saradnju u oblasti digitalne biologije u Evropi", trajanja od 01.03.2019. do 28.02.2023.

- Projekat od nacionalnog interesa PRIN-Ban 2017 kôd 2017J3E2W2_005: Osovina crijeva i jetre i crijevno-vaskularna barijera u homeostazi i bolesti (25.09.2019. do 24.09.2021.)

- Projekat HORIZON 2020 – H2020-INFRADEV-2019-2, tip aktivnosti: RIA, skraćenica „*ELIXIR-CONVERGE*", naslov projekta: Povezivanje i poravnavanje *ELIXIR* čvorova radi obezbjeđivanja održivih usluga menadžmenta podataka u biološkim naukama, po načelu *FAIR* (podaci su: pronalazivi, dostupni, interoperabilni i ponovo upotrebljivi – pri. prev.). SPORAZUM O STIPENDIRANJU broj: 871075 (od 01.02.2020. do 31.01.2023).

Odgovorno lice za CNR naučne aktivnosti i CNR infrastrukturu:

-Glavna istraživačica za naučne aktivnosti Medicinskog odsjeka: Proučavanje progresivnog ciklusa normalnih i malignih ćelija: uloga tumor-supresora p53 članova porodice.

- Laboratorija za molekularnu i ćelijsku biologiju

- Laboratorijska platforma za genomsko sekvenciranje FLX sistem 454

DODATNE INFORMACIJE

- Ekspertica za unutrašnju kontrolu evaluacije Ministarstva za obrazovanje, Ministarstva za univerzitet i istraživanje

- Članica Redakcijskog odbora Američkog žurnala za translaciona istraživanja

- Članica Redakcijskog odbora za molekularnu i ćelijsku onkologiju žurnala „Pomjeranje granica u ćelijskoj i istraživačkoj biologiji i granica u onkologiji" (od 21.02.2019)

- Glavna i odgovorna za proceduru nacionalne registracije Nacionalnog istraživačkog savjeta Italije CNR, RUP čl. 31 Zakonodavnog dekreta 18. april 2016, b. 50 u kategoriji „Usluge i snabdijevanje – 2A* : prva zagrada": RUP odobren za procedure u iznosu jednakom ili većem od € 40,000.00".

- Članica Istraživačkih odbora Nacionalnog istraživačkog savjeta Italije (CNR)

- Članica Naučnog komiteta i voditeljica radionica

- Radionica za sekvenciranje sledeće generacije – Bari 16.-18. septembar 2009. (http://mi.caspur.it/workshop_NGS09/)

- Radionica za sekvenciranje sledeće generacije – treće izdanje - Bari 12.-14. oktobar 2011. (http://caspur.it/workshop_NGS11)

- Ažuriranje u endokrinologiji i pedijatrijskoj dijabetologiji - Bari 13.-14. oktobar 2017. (http://www.meeting-planner.it/events/update-endocrinologia-diabetologia-pediatrica)

- 1. Nacionalni kongres nutrigenomike i nutricionizma - Bari 12.-13. oktobar 2018. (http://nutrigenomica.ba.itb.cnr.it)

- Voditeljica obuke „Bezbjednost hrane i nutricionizam: hrana koja čini razliku, od proizvodnje do potrošnje" – Konferencijska sala Trgovinske komore - Bari 19.12.2019.

- Recenzentkinja za nekoliko međunarodnih specijalizovanih publikacija uključujući sledeće: Kanceri, Molekularna karcinogeneza, EBioMedicina, Terapeutika i kliničko upravljanje rizicima, OnkoTargetiranje i terapija, Pomjeranje granica u ćelijskoj i razvojnoj biologiji i granica u onkologiji.

Članica naučnih udruženja:

- Nacionalna asocijacija biologa Italije, Specijalni registar biologa

- Italijansko udruženje za biofiziku i molekularnu biologiju

- Italijansko udruženje za celularnu biologiju i diferencijaciju

- Publikacije:

- Publikacije u međunarodnim žurnalima: 42

- Publikacije u nacionalnim žurnalima: 4

- Poglavlja u knjigama (međunarodni urednici): 4

PATENT „Metoda preparacije i amplifikacije reprezentativnih i specificiranih biblioteka lanaca kDNK za visokopropusno sekvenciranje (pronalazači: Apollonia Tullo, Marina Mangiulli, Elisabetta Sbisà, Graziano Pesole – Patent BR.°11738288.7 – 1406 / 2576780)

GLAVNE TEME ISTRAŽIVANJA: 1) proučavanje diferencijalne uloge p53 i njegovog relativa p63/p73 u kontroli ćelijske proliferacije; **2)** proučavanje mehanizama koji izazivaju aktiviranje i deaktiviranje proteina p53 i njegovih relativa p63 i p73; **3)** genomičko i transkriptomičko proučavanje primjenom tehnologija sekvenciranja sledeće generacije (NGS); **4)** proučavanje poremećaja rasta u djece.

Doljepotpisana izjavljuje da je saglasna sa obradom njenih ličnih podataka, u skladu sa Pravosudnim dekretom od 30. juna 2003, b. 196, radi ispunjavanja zahtjeva vezanih za predmetnu prijavu.

Doljepotpisana je svjesna da je davanje lažnih izjava, netačnost podataka i upotreba lažnih isprava kažnjivo shodno krivičnom zakoniku i specijalnim relevantnim zakonima.

U skladu sa Predsjedničkim dekretom Italije D.P.R. br. 445/2000, italijanski potpis ne podliježe ovjeri; predmetna izjava mora biti propraćena fotokopijom lične isprave.

Bari, 23.07.2020.

dr Apollonia Tullo

APOLLONIA TULLO

27.08.2020.

15:39:52 Koordinisano svjetsko vrijeme (UTC)

Prezime TULLO

Ime APOLLONIA

Rođena 10.09.1962.

Akt br. 204p I S A

u Modunju (MODUGNO) (BA)

Državljanstvo ITALIJANSKO

Prebivalište MODUNJO

Ulica LUCCA. 15

Bračno stanje = = = =

Zanimanje ISTRAŽIVAČICA

LIČNI ZNACI RASPOZNAVANJA

Visina 1.62

Boja kose SMEĐA

Boja očiju SMEĐA

Osobeni znaci .....

Naplaćene takse 5.42

[fotografija – prim. prev.]

Svojeručni potpis

U Modunju 08.08.2013.

Otisak prsta - lijevi kažiprst

[potpis i pečat – prim. prev.]

ISTIČE 10.09.2023.
AS 7389526
REPUBLIKA ITALIJA
OPŠTINA MODUNJO (MODUGNO)
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BR. AS 7389526
PRIPADA
TULLO
APOLLONIA

NACIONALNI ISTRAŽIVAČKI SAVJET

INSTITUT ZA BIOMEMBRANE, BIOENERGETIKU I MOLEKULARNE BIOTEHNOLOGIJE

DIREKTOR
ULICA VIA AMENDOLA 122/O – 70126 BARI (ITALIJA)
TEL. (+39)-080-5929818

UPUĆENO NADLEŽNIM ODGOVORNIM LICIMA

Ja, doljepotpisani dr Serđo Đanatazio (izvorno: Dr. Sergio Giannattasio – prim. prev.) u svojstvu vršioca dužnosti direktora Instituta za biomembrane, bioenergetiku i molekularne biotehnologije (IBIOM) u Nacionalnom istraživačkom savjetu Italije ovim izjavljujem da je dr Apolonija Tulo (izvorno: Dr. Apollonia Tullo – prim. prev.) (CNR-ID br. 656) stalno zaposlena na radnom mjestu istraživačice u IBIOM-u, gdje sprovodi istraživanje i napredne obuke u skladu sa naučnom autonomijom, zagarantovanom Evropskom poveljom za istraživače.

dr Serđo Đanatazio (izvorno: Dr. Sergio Giannattasio – prim. prev.)

(Vršilac dužnosti direktora IBIOM-a)

GIANNATTASIO

SERGIO

28.08.2020.

08:42:21 Koordinisano svjetsko vrijeme (UTC)

Curriculum Vitae

PERSONAL INFORMATION	Apollonia Tullo
Address	Institute of Biomembrane, Bioenergetics and Molecular Biotechnology (IBIOM) –Bari - CNR, -Via Amendola 122/D 70126 Bari, Italy
Codice Fiscale	TLLPLN62P50F262E
Telephone	0039-080-5929672 E-mail : a.tullo@ibiom.cnr.it

WORK EXPERIENCE

1994 to date	CNR Researcher at Institute of Biomembrane, Bioenergetics and Molecular Biotechnology (IBIOM) –Bari - CNR
2020	Member of the Scientific Committee of the Foresight Health group as part of the CNR S&T Foresight project in order to promote initiatives that can help to define research strategies capable of addressing major social challenges, such as energy, food, health, water.
2020	Member of the Scientific Committee 2nd level Master in "Integrated medicine and food management for cancer prevention and treatment" - Department of Medicinal Sciences - University of Catania.
2018	Member of PhD Academic Board of Functional and Applied Genomics and Proteomics – University of Bari
2017	Full Professor qualification in Molecular Biology - National Scientific Qualification (ASN)
2015 to 2017	Contract Professor of Molecular Biology (Bachelor in Medicine and Surgery- University of Bari)
2008 to 2015	Contract Professor of Laboratory of Molecular Biology and Bioinformatics (Faculty of Biotechnology – University of Bari)
2000	Invited researcher at Prof. Sir David Lane Laboratory of the Cancer Research Campaign, Dept. of Surgery and Molecular Oncology – University of Dundee – Scotland
1999 to date	Tutor of Degree thesis, fellowships, training and PhD students
1993-1994	CNR fellowship
1992-1993	EMBO (European Molecular Biology Organization) Fellowship at the Institut fur Tumorbiologie-Krebsforschung – Dr. Karwan laboratory

University of Wien (Austria)

EDUCATION AND TRAINING

2009	NGS (Next Generation Sequencing) 454 GS FLX Titanium Series (Roche) training
2001	Flow cytometry Training of Becton Dickinson FACSCaliburTM
1997	Master in Clinic and Laboratory Oncology: new frontiers in Biotechnology and in therapy of neoplasia
1993	PhD degree in Biochemistry and Molecular Biology
1988	Professional examination as biologist
1986	Degree in Biological Sciences (summa cum laude) at the University of Bari

SCIENTIFIC ACTIVITIES

Research Projects Responsible

- Research Unit I Project PIR01_00017 CNRBiOmics "Strengthening of a platform for the high throughput production of "omic" data" (National Bioinformatics Research Center for the "Omics" Sciences) (2019-2021)
- Research Unit Interomics project (2017-2018): "Scouting cross-kingdom transfer: effect of exogenous plant microRNA on the expression of human genes involved in ageing-related diseases"
- Research Unit Progetto n.57, prot.AOO_044 del 14/12/2009-0015366-0008015, BioBancOncologicaPugliese (BioBOP) – Network for the use of controlled oncological tissues e characterized by the development of new diagnostic approaches, pharmacological and biomedical" (2009-2013)
- Caripuglia project 2011-2012 "Development of a new anti-tumour therapy based on a biopeptide able to restore p53 oncosuppressor activity"
- Research Unit PRIN Project 2007

Participation to other research projects

- PRIN (1999-2000) Bioinformatics and Genomic research

- Science and Technology Network Strengthening Plans MURST Cluster C03 (2000-2002)

- Extraordinary contribution referred to D.M. n. 1105 del 9.10.02 MIUR. National Operational Program "Scientific Research, Technological Development, Higher Education " 2000/2006

- PNR 2001-2003 (FIRB art.8) D.M.199, Strategic Program: Post-genome, grant 31-063933; Research and Development of new bioinformatics and Biotechnology instruments for the analysis of gene and protein expression profile of cancer and for the identification of biological markers to early diagnoses of colorectal, kidney and oral cavity neoplasia" (2006-2009

- FIRB 2003 art. 8 D.D. 2187 del 12-12-2003; Protocol: RBLA039M- LIBI: International Laboratory for Bioinformatics (2005-2010)

- Progetto FAR LAB. N. 8 "Public Private laboratory for Bioinformatics applied to Genomics" DM19410 (2007-2010)

- Research Project FISM "High-throughput investigation of Multiple Sclerosis associated infectious agents by unbiased cDNA deep-sequencing" (2008-2009)

- PON01_01297 VIRTUALB - Advanced systems of biomedical mechatronics for diagnosis and medical therapy based on Virtual and Augmented Reality, microelectronics, and robotic laboratories with high throughput.

- PON01_02589 "Development of a multiplex technological platform for molecular diagnostics, portable and automated, based on the instrumental logic of the Lab-on-chip, capable of allowing multiparametric applications in the infectious field". Acronym: "MicroMap" .

- Bilateral Italy-Montenegro Project "Mitochondrial dysfunction in cancer growth, drug resistance and chemotherapy induced neuropathy" IBIOM-University of Montenegro, Faculty of medicine and surgery Podgorica (2017-2018).

- Progetto POR Puglia FESR-FSE 20142020 Action 1.6. Announcement "Innonetwork", cod. IJLZKD0, A.D. n.124 del

16/10/2017: "OMICS4FOOD "Improvement in the production processes of fresh food produced from flour through approaches based on omic technologies and complex information, elaborated by an information system designed and developed in a Cloud environment" (2018-2020).

- Project of the Ministry of Sciences of Montenegro "New methods for risk stratification for the progression of cancer and Alzheimer's disease in patients in Montenegro (DEMONSTRATE)" (1-04-2019 – 31-03-2021)

- Research Project "IDF SHARID – Innovative Devices for SHAping the RIsk of Diabetes", codice identificativo ARS01_01270 within the Industrial Research and Experimental Development in the 12 areas of specialization identified by PNR 2015-2020.

- Industrial research and experimental development project in the 12 areas of specialization identified by the PNR 2015-2020 "BIOMIS" - Establishment of the biobank of the intestinal microbiota and human salivary: from dysbiosis to symbiosis "identification code ARS01_01220 (from 01-07-2018 to 30- 06-2021).

- Project HORIZON 2020 - H2020-INFRAEOSC-2018-2020. INFRAEOSC-04-2018. RIA, Proposal Number: SEP-210489595, Acronym "EOSC-LIFE", Number 824087 – Project title "Providing An Open Collaborative Space For Digital Biology In Europe" durata dal 01/03/2019 al 28/02/2023.

- Project PRIN-Ban 2017 code 2017J3E2W2_005: Gut-liver axis and the gut vascular barrier in homeostasis and disease (25-09-2019 al 24-09-2021).

- Progetto HORIZON 2020 - H2020-INFRADEV-2019-2, Type of Action: RIA, Acronym "ELIXIR-CONVERGE", Project title: Connect and align ELIXIR Nodes to deliver sustainable - FAIR life-science data management services. GRANT

AGREEMENT Number: 871075 (dal 1-02-2020 al 31-01-2023).

Responsible of CNR Scientific Activities and CNR infrastructures:

- Principal Investigator of the Scientific Activity for the Medicine Department: Study of the normal and malignant cell cycle progression: the role of the tumour-suppressor p53 family members
- Molecular and Cellular Biology Laboratory
- Genome Sequencer FLX System 454 Platform Laboratory

FURTHER INFORMATIONS

- Auditor Expert for MIUR (Ministry of Education Ministry of University and Research) evaluation

- Member of the Editorial Board of the American Journal of Translational Research

- Member of the Editorial Board of the Molecular and Cellular Oncology of the Journal Frontiers in Cell and Developmental Biology and Frontiers in Oncology (from 21-02-2019)

- Suitable within the CNR National Register of the RUP (Unique Responsible for the Procedure) art. 31 of Legislative Decree 18 April 2016, n. 50 to the category 'Services and supplies - 2A *: first bracket': RUP Enabled for procedures of an amount equal to or less than € 40,000.00 ".

- Member of CNR Examination boards

- Scientific Committee Member and Workshop Moderator

- Next Generation Sequencing Workshop – Bari 16-18 settembre 2009 (http://mi.caspur.it/workshop_NGS09/)
- Next Generation Sequencing Workshop- Third Edition – Bari 12-14 ottobre 2011(www.caspur.it/workshop_NGS11)

- Update in Endocrinologia e Diabetologia Pediatrica – Bari 13-14 ottobre 2017 (http://www.meeting-planner.it/events/update-endocrinologia-diabetologia-pediatrica/)
- 1° National Congress in Nutrigenomics and Nutrition – Bari 12-13 Ottobre 2018 (http://nutrigenomica.ba.itb.cnr.it)
- Moderator Training course "Food safety and nutrition: food that makes the difference, from production to consumption" - Chamber of Commerce Conference Room - Bari 19-12-2019.

- **Reviewer for several international journals** including, Cancers, Molecular Carcinogenesis, EBioMedicine, Therapeutics and Clinical Risk Management, OncoTargets and Therapy, Frontiers in Cell and Developmental Biology and Frontiers in Oncology.

Membership of Scientific Society
- Ordine Nazionale dei Biologi, Elenco Speciale Biologi
- Italian Society of Biophysics and Molecular Biology
- Italian Society of Cellular Biology and Differentiation

- **Publications**
- Pubblications in international journals: 42
- Pubblications in national journals: 4
- Chapters in books (international editors): 4

PATENT "Method for the preparation and amplification of representative and strand-specific libraries of cDNA for high throughput sequencing" (Inventors: Apollonia Tullo, Marina Mangiulli, Elisabetta Sbisà, Graziano Pesole –Patent N°11738288.7 – 1406 / 2576780)

MAJOR RESEARCH TOPICS : 1) study of the differential role of p53 and its relative p63/p73 in the control of cell proliferation; 2) study of the mechanisms that lead to the activation and de-activation of p53 protein and of its relatives p63 and p73; 3) genomic and transcriptomic study through the application of the NGS technologies (Next Generation Sequencing); 4)study of growth failure in children.

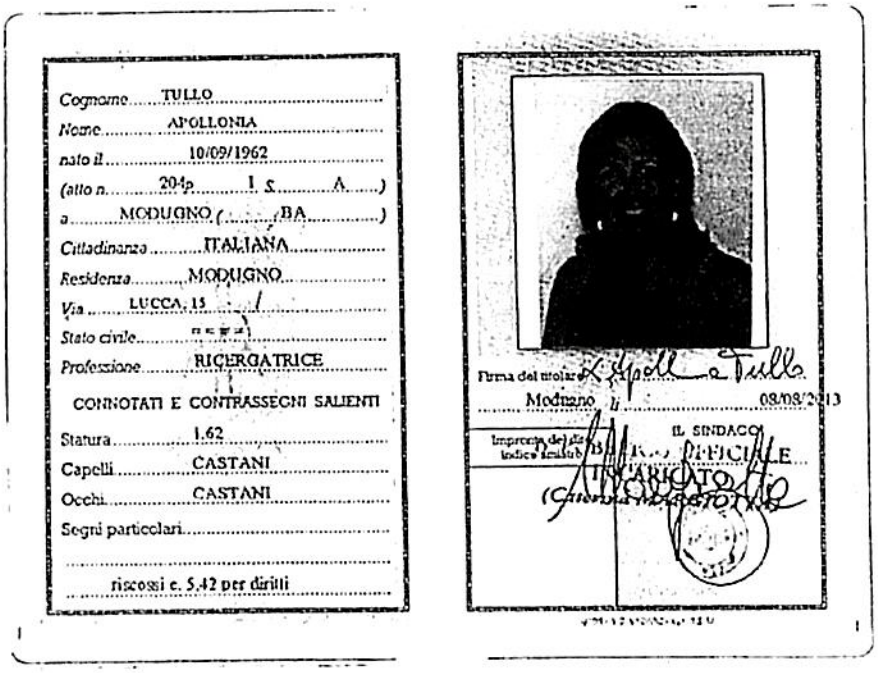
The undersigned express their consent for the personal data provided to be processed, in compliance with the Legislative Decree 30 June 2003, n. 196, for the obligations related to the present application. The undersigned is aware that, pursuant to art. 76 of the D.P.R. n. 445 of the 28/12/2000, the false declarations, the falsity in the records and the use of false deeds are punished according to the penal code and the special laws in matter.

In accordance with the Italian DPR no. 445/2000, Italian the signature is not subject to authentication, this declaration must be accompanied by a photocopy of an identification document.

Bari, 23-07-2020

Dr. Apollonia Tullo

APOLLONIA TULLO
27.08.2020
15:39:52 UTC



Cognome TULLO
Nome APOLLONIA
nato il 10/09/1962
(atto n. 204 p. I S. A.)
a MODUGNO (BA)
Cittadinanza ITALIANA
Residenza MODUGNO
Via LUCCA, 15
Stato civile
Professione RICERCATRICE

CONNOTATI E CONTRASSEGNI SALIENTI

Statura 1.62
Capelli CASTANI
Occhi CASTANI
Segni particolari

riscossi e. 5.42 per diritti

Firma del titolare Apollonia Tullo
Modugno li 08/08/2013
IL SINDACO
L'UFFICIALE
L'ARICATO

SCADE IL 10/09/2023

AS 7389526

REPUBBLICA ITALIANA

COMUNE DI
MODUGNO
CARTA D'IDENTITA
N° AS 7389526
DI
TULLO
APOLLONIA

Consiglio Nazionale delle Ricerche

ISTITUTO DI BIOMEMBRANE , BIOENERGETICA E BIOTECNOLOGIE MOLECOLARI

IL DIRETTORE

VIA AMENDOLA 122/O – 70126 BARI (ITALY)
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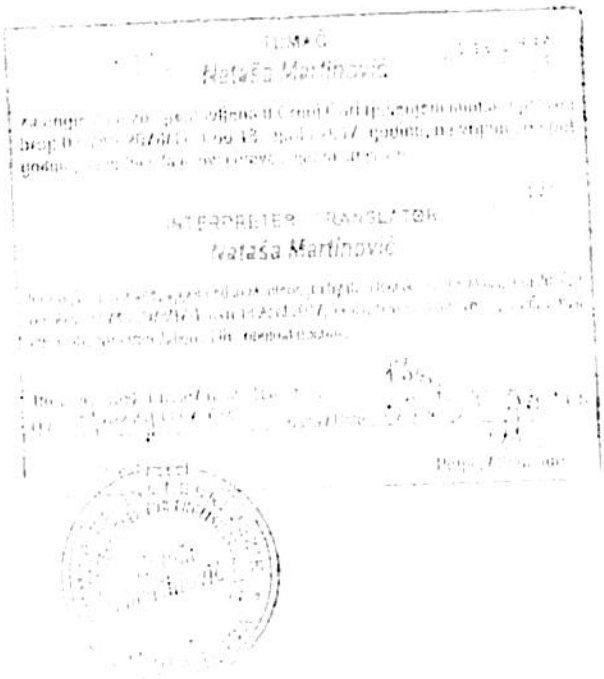
TO WHOM IT MAY CONCERN

I, the undersigned Dr. Sergio Giannattasio in my capacity of Acting Director of the Institute of Biomembranes, Bioenergetics and Molecular Biotechnologies (IBIOM) of the National Research Council of Italy, hereby certify that Dr. Apollonia Tullo (CNR-ID No. 656) has a permanent position as a Researcher at IBIOM where she carries out research and advanced training activities in compliance with the scientific autonomy guaranteed by the European Charter for Researchers.

Dr. Sergio Giannattasio
(*Acting Director of IBIOM*)
GIANNATTASIO
SERGIO
28.08.2020
08:42:21 UTC



1) E. Sbisa', M. Nardelli, F. Tanzariello, A. Tullo and C. Saccone
The complete and symmetric transcription of the main non coding region of rat mitochondrial genome: in vivo mapping of heavy and light transcripts.
Current Genetics, 1990, 17: 247-253
IF= 1,889

2) E. Sbisa', A. Tullo, M. Nardelli, F. Tanzariello And C. Saccone
Trascription mapping of the Ori L region reveals novel precursors of mature RNA species and antisense RNAs in rat mitochondrial genome.
FEBS Letters 1992, 296: 311-316
IF= 3.720

3) M. Nardelli, S. Tommasi, A.M. D'Erchia, F. Tanzariello, A. Tullo, A.T. Primavera, M. De Lena, E. Sbisa' And C. Saccone
Detection of novel transcripts in the human mitochondrial DNA region coding for ATPase8-ATPase6 subunits.
FEBS Letters, 1994, 344: 10-14
IF=3,720

4) A. Tullo, F. Tanzariello, A. M. D'Erchia, M. Nardelli, P. A. Papeo, E. Sbisa' And C. Saccone
Transcription of rat mitochondrial NADH-dehydrogenase subunits Presence of antisense and precursor RNA species.
FEBS Letters, 1994, 354: 30-36
IF= 3.720

5) A. Tullo, W. Rossmanith, E.M. Imre, E. Sbisa', C. Saccone and R.M.Karwan
RNase mitochondrial RNA processing cleaves RNA from the rat mitochondrial displacement loop at the origin of heavy-strand DNA replication.
Eur. J. Biochem, 1995, 227: 657-662
IF= 3,307

6) W. Rossmanith, A. Tullo, T. Potuschak , R. M. Karwan and E. Sbisa'
Human mitochondrial tRNA processing.
J. Biol. Chem., 1995, 270: 1-7
IF= 7,666

7) E. Sbisa', G. Pesole, A. Tullo and C. Saccone
The evolution of the RNAase P and RNase MRP associated RNAs: phylogenetic analysis and nucleotide substitution rate
J. Mol. Evol.1996, 43: 46-57
IF= 3,655

8) K. Honda, E. Sbisa', A. Tullo, P.A. Papeo, C. Saccone, S. Poole, M. Pignatelli, R.R. Mitry, S. Ding, A. Isla, R. Brancatisano, A. Davies, N.A. Habib (The three first authors had equal contribution to this study)
p53 mutations is a poor prognostic indicator for survival in patients with hepatocellular carcinoma undergoing surgical tumour ablation
British Journal of Cancer,1998, 77: 776-782

first-co-authorship with Honda and Sbisà IF= 5.082

9) D'Erchia A.M, Pesole G., Tullo A., Saccone C., Sbisa' E.
Guinea pig p53 mRNA: identification of new elements in coding and untranslated regions and their functional and evolutionary implications
Genomics, 1999, 58: 50-64
IF= 3.386

10) Tullo A., D'Erchia A.M., Honda K., Mitry R.R., Kelly M.D., Habib N.A., Saccone C., Sbisa' E.
Characterization of p53 mutations in Colorectal Liver Metastases and correlation with clinical parameters
Clin Cancer Res, 1999, 5: 3523-3528
IF= 7,837

11) Tullo A., D'Erchia A.M., Honda K., Kelly M.D., Habib N.A., Saccone C., Sbisa', E.
New p53 mutations in hilar cholangiocarcinoma
Eur J Clinical Investigation. 2000, 30: 798-803
IF = 2.071

12) Havlik R. Sbisa', E., Tullo A., Kelly M.D., Mitry R.R., Jiao L., R. Mansour M. R., Honda K., Habib N.A.
Results of resection for hilar cholangiocarcinoma with analysis of prognostic factors
Hepato-Gastroenterology. 2000, 47: 927-31
IF=0,9

13) Tullo A., Sbisa', E.
Molecular characterization of p53 mutations in primary and secondary liver tumors: diagnostic and therapeutic perspectives
Molecular Biotechnology, 2002, 21: 265-278
IF = 1

14) Saccone C., Barome P.O., D'Erchia A.M., D'Errico I., Pesole G., Sbisa' E., Tullo A.
Molecular Strategies in Metazoan Genomic Evolution
Gene, 2002, 300: 195-201
IF= 2.778

15) D'Erchia A.M., Tullo A., Pesole G., Saccone C., Sbisa', E.
p53 gene family:structural, functional and evolutionary features
Current Genomics, 2003, 4: 13-26
IF= 1.077

16) Tullo A, D'Erchia A.M., Sbisa', E.
Methods for screening tumours for p53 status and therapeutic exploitation
Expert Review of Molecular Diagnosis, 2003, 3 :289-301
IF= 4.089

17) Tullo A., Mastropasqua G., Bourdon J.C., Centonze P., Gostissa M., Costanzo A., Levrero M., Del Sal G., Saccone C., Sbisa' E.

Adenosine deaminase, a key enzyme in DNA precursors control, is a new p73 target.
Oncogene 2003, 22 : 8738-8748
IF=7.357

18) Sbisà E., Mastropasqua G., Lefkimmiatis K., Caratozzolo M.F., D'Erchia A.M., Tullo A
Connecting p63 to cellular proliferation: the example of the Adenosine Deaminase target gene
Cell Cycle, 2006, 5: 205-212
IF= 5,243

19) D'Erchia A.M., Tullo A, Lefkimmiatis K., Saccone C., Sbisà E.
The Fatty Acid Synthase Gene is a Conserved p53 Family Target from Worm to Human.
Cell Cycle. 2006, 5: 750-758
IF= 5,243

20) Sbisà E, Catalano D, Grillo G, Licciulli F, Turi A, Liuni S, Pesole G, De Grassi A, Caratozzolo Mf, D'erchia Am, Navarro B, Tullo A, Saccone C, Gisel A
p53FamTaG : a database resource of human p53, p63 and p73 direct target genes combining in silico prediction and microarray data
BMC Bioinformatics 2007, 8 (Suppl I):520
IF= 3,493

21) Mangiulli M, Valletti A, Caratozzolo MF, Tullo A, Sbisà E, Pesole G, D'Erchia AM
Identification and functional characterization of two new transcriptional variants of the human p63 gene.
Nucleic Acids Res. 2009 (Q1) Aug 21Volume: 37 Issue: 18 Pages: 6092-6104
IF 2009= 8,278

22) Lefkimmiatis K, Caratozzolo MF, Merlo P, D'Erchia AM, Navarro B, Levrero M, Sbisa' E, Tullo A.
p73 and p63 sustain cellular growth by transcriptional activation of cell cycle progression genes.
Cancer Res. 2009 (Q1) Nov 15;69(22):8563-71. doi: 10.1158/0008-5472.CAN-09-0259. Epub 2009 Oct 27.
IF 2009= 8.65

23) MF Faienza, F Marzano, MF Caratozzolo, E Sbisà, L Cavallo , A Tullo
Study of the regulation of the IGFBP3 gene expression in short children born small for gestational age
Hormone research (2009) 72 (suppl 3): 438-439
IF 2009= 2,48

24) - Valenti D, Tullo A, Caratozzolo MF, Merafina RS, Scartezzini P, Marra E, Vacca RA.
Impairment of F1F0-ATPase, adenine nucleotide translocator and adenylate kinase causes mitochondrial energy deficit in human skin fibroblasts with chromosome 21 trisomy.
Biochem J. 2010 Sep 28;431(2):299-310.
IF=5,016 (4,779 al 2015)

25) - Valletti A, Anselmo A, Mangiulli M, Boria I, Mignone F, Merla G, D'Angelo V, Tullo A, Sbisà E, D'Erchia AM, Pesole G

Identification of tumor-associated cassette exons in human cancer through EST-based computational prediction and experimental validation.
Mol Cancer. 2010 (Q1) Sep 2;9:230.
IF=5,4

26) - Faienza MF, Marzano F, Ventura AM, Wasniewska M, Valenzise M, Valletti A, Caratozzolo MF, Cornacchia S, Sbisà E, Cavallo L, Tullo A.
Regulation of IGFBP3 gene expression in short children born small for gestational age.
Growth Horm IGF Res. 2011 Dec;21(6):349-55.
IF= 2,164

27) - Caratozzolo MF, Micale L, Turturo MG, Cornacchia S, Fusco C, Marzano F, Augello B, D'Erchia AM, Guerrini L, Pesole G, Sbisà E, Merla G, Tullo A.
TRIM8 modulates p53 activity to dictate cell cycle arrest.
Cell Cycle, (Q2) 2012, Feb 1;11(3):511-23.
IF=5,359

28) - Vieux-Rochas M, Bouhali K, Mantero S, Garaffo G, Provero P, Astigiano S, Barbieri O, Caratozzolo MF, Tullo A, Guerrini L, Lallemand Y, Robert B, Levi G, Merlo GR.
BMP-mediated functional cooperation between Dlx5;Dlx6 and Msx1;Msx2 during mammalian limb development.
PLoS One. 2013;8(1)
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