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Broj: 884/5-1
Podgorica, 18.06.2024. 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 8. Vodiča za doktorske studije, u prilogu akta dostavljamo obrazac D2 uz Predlog Odluke Vijeća o imenovanju Komisije za ocjenu doktorske disertacije dr med Jelene Vučinić, pod nazivom „Medjusobna korelacija gustine tumor-infiltrišućih limfocita CD4 i CD8 pozitivnih limfocita i PD-L1 ekspresije i njihova povezanost sa patološkim prognostičkim parametrima u molekularnim podtipovima ranog karcinoma dojke“ 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	Mr sci. Jelena (Darko) Vučinić		
Fakultet	Medicinski fakultet Podgorica		
Studijski program	Medicina		
Broj indeksa	2/19		
NAZIV DOKTORSKE DISERTACIJE			
Na službenom jeziku	„Međusobna korelacija gustine tumor-infiltrišućih limfocita, CD4 i CD8 pozitivnih limfocita i PD-L1 ekspresije i njihova povezanost sa patološkim prognosičkim parametrima u molekularnim podtipovima ranog karcinoma dojke“		
Na engleskom jeziku	"Correlation between the density of tumor-infiltrating lymphocytes, CD4 and CD8 positive lymphocytes and PD-L1 expression and their association with pathological prognostic parameters in molecular subtypes of early breast cancer"		
Naučna oblast	Histopatologija		
MENTOR/MENTORI			
Prvi mentor	Prof. dr Ljiljana Vučković	Medicinski fakultet Univerziteta Crne Gore	Histologija i embriologija
Drugi mentor			
KOMISIJA ZA PREGLED I OCJENU DOKTORSKE DISERTACIJE			
Prof. dr Filip Vukmirović		Medicinski fakultet Univerziteta Crne Gore	Patologija
Prof.dr Ljiljana Vučković		Medicinski fakultet Univerziteta Crne Gore	Histologija i embriologija
Prof.dr Dragana Tegeltija		Medicinski fakultet Univerziteta u Novom Sadu	Patologija
Datum značajni za ocjenu doktorske disertacije			
Sjednica Senata na kojoj je data saglasnost na ocjenu temu i kandidata	15.04.2022. godine		

Dostavljanja doktorske disertacije organizacionoj jedinici i saglasanost mentora	29.04.2024. godine
Sjednica Vijeća organizacione jedinice na kojoj je dat predlog za imenovanje komisija za pregled i ocjenu doktorske disertacije	14.06.2024. 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. Jelena Vučinić, Ljiljana Vučković, Janja Raonić. Correlation between stromal Th and Tc lymphocytes and PD-L1 expression in early breast cancer tumors. Folia Histochem Cytobiol. 2023; 61(4):193-204 doi:10.5603/fhc.97855

Obrazloženje mentora o korišćenju doktorske disertacije u publikovanim radovima

Dio istraživačkog materijala, koji proističe iz doktorske disertacije, publikovan je u vidu rada 2023. godine u renomiranom međunarodnom časopisu "Folia Histochemica et Cytobiologica", koji je indeksiran i nalazi se na SCIE listi (impakt faktor 1.5, kategorija Q2).

Pomenuta publikacija bila je fokusirana na ispitivanje povezanosti između imunohistohemijske ekspresije PD-L1 proteina i drugih parametara imunološkog odgovora (gustine i sastava stromalnog limfocitnog infiltrata i karakteristika peritumorskih limfoidnih agregata) u različitim molekularnim podtipovima ranog karcinoma dojke. Pored problematične prognostičke i prediktivne vrijednosti u karcinomu dojke, PD-L1 trenutno predstavlja jedini biomarker na osnovu kog se vrši selekcija pacijentkinja za imunološku terapiju, a u momentu sprovođenja doktorskog istraživanja inhibitori imunoloških kontrolnih tačaka bili su odobreni od strane Evropske agencije za ljekove, kao i Agencije za hranu i ljekove Sjedinjenih Američkih Država isključivo u terapiji uznapredovalog, neresektabilnog i metastatskog karcinoma dojke trostruko-negativnog molekularnog podtipa.

Rezultati navedenog istraživanja ukazali su na postojanje snažne pozitivne korelacije između PD-L1 ekspresije i gustine stromalnog limfocitnog infiltrata, kao i prisustva peritumorskih limfoidnih agregata u tumorskoj mikrookolini, nezavisno od molekularnog podtipa tumora. Takođe, identifikovana je statistički značajna asocijacija između PD-L1 pozitivnosti i većeg apsolutnog broja CD4 i CD8 limfocita u tumorskoj stromi, a po prvi put, upotrebom statističkih metoda utvrđena je granična vrijednost gustine stromalnog limfocitnog infiltrata (53%) iznad koje se prisustvo PD-L1 ekspresije može predvidjeti sa visokom dijagnostičkom tačnošću.

Dobijeni rezultati su od velikog značaja jer ukazuju na to da bi gustina stromalnog limfocitnog infiltrata mogla biti bolji prediktor PD-L1 pozitivnosti u ranom karcinomu dojke nego što je to molekularni podtip tumora i da bi, u cilju optimizacije upotrebe PD-L1 kao biomarkera u karcinomu dojke, interpretaciju njegove ekspresije trebalo staviti u kontekst intra- i peritumorskog limfocitnog infiltrata.

Datum i ovjera (pečat i potpis odgovorne osobe)
U Podgorici, (navesti datum) DEKAN Prof. dr Miodrag Radunović MP

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

UNIVERZITET CRNE GORE

MEDICINSKI FAKLTET

Broj: 670/1

Podgorica 29.04.2024. godine

P O T V R D A

Potvrđuje se da je dr med Jelena Vučinić , predala 7 primjeraka doktorske disertacije, pod nazivom „ **Međusobna korelacija gustine tumor-infiltrišućih limfocita ,CD4 i CD8 pozitivnih limfocita i PD-L1 ekspresije i njihova povezanost sa patološkim prognostičkim parametrima u molekularnim podtiovima ranog karcinoma dojke" dana 29.04.2024**.godine (Broj protokola 670) .

Potvrda se izdaje u svrhu pregleda i ocjene doktorske disrtacije.

ŠEF STUDENTSKE SLUŽBE

Sonja Vukićević,diplomirani pravnik

UNIVERZITET CRNE GORE
MEDICINSKI FAKULTET
Broj: 884/5
Podgorica, 14.06.2024. 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: 670/1 od 17.05.2024. godine i tačke 3.8 Vodiča za doktorske studije Univerziteta Crne Gore, Vijeće Medicinskog fakulteta na elektronskoj sjednici održanoj 13-14.06.2024. godine, donijelo je

O D L U K U

I

Kandidat dr med Jelena Vučinić, ispunjava formalne uslove za ocjenu doktorske disertacije: „**Medjusobna korelacija gustine tumor-infiltrišućih limfocita CD4 i CD8 pozitivnih limfocita i PD-L1 ekspresije i njihova povezanost sa patološkim prognostičkim parametrima u molekularnim podtipovima ranog karcinoma dojke**".

II

Predlaže se Komisija za ocjenu doktorske disertacije dr med Jelene Vučinić, pod navedenim nazivom: „**Medjusobna korelacija gustine tumor-infiltrišućih limfocita CD4 i CD8 pozitivnih limfocita i PD-L1 ekspresije i njihova povezanost sa patološkim prognostičkim parametrima u molekularnim podtipovima ranog karcinoma dojke**" u sastavu:

1. **Prof. dr Filip Vukmirović**, redovni profesor Medicinskog fakulteta Univerziteta Crne Gore, naučna oblast: patologija;
2. **Prof. dr Ljiljana Vučković**, redovna profesorica Medicinskog fakulteta Univerziteta Crne Gore, naučna oblast: patologija;
3. **Prof. dr Dragana Tegeltija**, vanredna profesorica Medicinskog fakulteta Univerziteta u Novom Sadu, naučna oblast: patologija;

III

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

Obrazloženje

Dr med Jelena Vučinić je predala doktorsku disertaciju pod nazivom: **Medjusobna korelacija gustine tumor-infiltrišućih limfocita CD4 i CD8 pozitivnih limfocita i PD-L1 ekspresije i njihova povezanost sa patološkim prognostičkim parametrima u molekularnim podtipovima ranog karcinoma dojke**" dana 29.04.2024. godine.

Vijeće Medicinskog fakulteta je utvrdilo da kandidat ispunjava uslove iz člana 38 Pravila doktorskih studija, da kandidat dr med Jelena Vučinić 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

FOLIA HISTOCHEMICA
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ORIGINAL PAPER

VIA MEDICA

Correlation between stromal Th and Tc lymphocytes and PD-L1 expression in early breast cancer tumors

Jelena Vučinić[1, 2], Ljiljana Vučković[1, 2], Janja Raonić[1, 2]

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Abstract

Introduction. Prognostic and predictive value of PD-L1 as a biomarker in breast cancer remains controversial. While some studies suggest its association with negative prognostic parameters, others reported a highly significant association between PD-L1 expression and tumor-infiltrating lymphocytes, which are known to be an independent favorable prognostic factor. The aim of present study is to examine the relationship between immune response markers and PD-L1 expression in early breast cancer.

Material and methods. Immunohistochemical expression of PD-L1, along with density and composition of stromal lymphocytic infiltrate and peritumoral lymphoid aggregates was analyzed in 95 samples of invasive breast cancer.

Results. A strong positive correlation between PD-L1 expression and the density of stromal lymphocytic infiltrate and peritumoral lymphoid aggregates was identified and a cut-off value of 53% coverage of tumor stroma by lymphocytes, with which PD-L1 positivity can be predicted with excellent diagnostic accuracy, was determined for the first time using statistical methods. Additionally, PD-L1 positivity was observed significantly more often in tumors with higher absolute number of both CD4 and CD8 T-lymphocytes in the stromal infiltrate. No significant correlation with molecular subtype of breast cancer was found.

Conclusions. Our results indicate that the density of stromal lymphocytic infiltrate might be a better predictor of PD-L1 positivity in early breast cancer than the molecular subtype and that the key to the optimization of PD-L1 as a biomarker in breast cancer lies in its interpretation in the context of other immune response markers. *(Folia Histochemica et Cytobiologica 2023, Vol. 61, No. 4, 193–204)*

Keywords: PD-L1; early breast cancer; tumor-infiltrating lymphocytes; CD4 lymphocytes; CD8 lymphocyte; peritumoral lymphoid aggregates

Introduction

The importance of effective immune response in prevention of the development and progression of cancer has long been recognized [1] and huge efforts of the scientific community are still directed to the improvement of our understanding of the variety of mechanisms by which tumor cells manage to evade immune surveillance [2]. The immune system functions as a complex network of effector cells, molecules and biochemical processes whose main purpose is to defend the organism from foreign particles, while at the same time limiting autoreactivity and harmful effect of immune cells and the accompanying inflammatory process on the organism itself [3].

The immune system's response to the presence of tumor cells is reflected in the infiltration of the tumor by mononuclear immune cells, mainly different populations of T-lymphocytes, but also follicular dendritic cells, macrophages, B-lymphocytes and plasma cells, all together referred to as tumor-infiltrating lymphocytes (TILs) [4]. It has been believed that cytotoxic (CD8) T-lymphocytes, which eliminate tumor cells, after being activated by CD4 helper T-lymphocytes, either directly through the expression of Fas ligand on their surface or by releasing potent cytotoxins, are

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the key players in antitumor immune response [5]. On the other hand, CD4 lymphocytes have a much more complex role in mediation of the antitumor immune response because, depending on the predominant cytokines secreted in the tumor microenvironment, they can differentiate into different subpopulations of effector cells, displaying various properties [5].

An effective immune response relies directly on the fine balance between co-stimulatory and co-inhibitory signals mediated by members of the B7-1/B7-2-CD28/CTLA-4 protein superfamily [6–9]. One of the members of this superfamily is PD-1 molecule (programmed cell death receptor 1), a transmembrane protein that is expressed as a monomer on the surface of activated CD4 and CD8 T-lymphocytes, B-lymphocytes, NK-cells, monocytes and certain antigen-presenting cells [6, 10]. One of its ligands, PD-L1, is a transmembrane glycoprotein which in addition to its constitutive expression on the surface of inflammatory cells, can also be expressed on the surface of neurons, keratinocytes, syncytiotrophoblast cells, endocrine cells of the pancreatic islets, that is, in those tissues and organs where preservation of immune tolerance and prevention of the development of autoimmunity is of vital importance [11]. Signal transduction *via* PD-1/PD-L1 complex takes place in parallel with the establishment of contact between the T-cell receptor and the antigen presented as part of the major histocompatibility complex (MHC) molecule, with consequent effects on the cell cycle and metabolism of T-cells [2], which become anergic and enter the process of apoptosis [12].

So far, a large number of solid tumors that use this natural protection mechanism against the harmful effects of the immune responses and inflammation to avoid the immune surveillance of the organism, by expressing PD-L1 on the surface of tumor cells or inflammatory cells of the tumor microenvironment, have been identified [11, 13–15]. Therefore, the use of anti-PD-1/PD-L1 antibodies/inhibitors is one of the widely adopted therapeutic modalities in a large number of malignancies nowadays, primarily lung cancer [16–18].

Immune checkpoint inhibitor therapy in breast cancer, which is the most common malignancy and the leading cause of death from malignant diseases in female population worldwide [19], has so far found its place only in the treatment of triple-negative breast cancer (TNBC). A number of monoclonal antibodies to block the PD-1/PD-L1 axis have been approved by the United States Food and Drug Administration in the treatment of locally advanced, unresectable, and metastatic TNBC, as the most immunogenic subtype of breast cancer with potentially the greatest benefits from immunotherapy [20, 21].

On the other hand, the results of various studies suggest that a higher density of stromal tumor-infiltrating lymphocytes (sTILs), as well as the presence of peritumoral lymphoid aggregates [22], are indicators of a favorable response to chemotherapy and a generally better prognosis, not only in triple-negative (TNBC), but also in non-luminal HER-2 positive breast cancers [23, 24]. The latter two subtypes of breast cancer have been identified as tumors that show high expression of PD-L1 protein more often compared to luminal molecular subtypes [25].

However, a review of the literature reveals a large number of studies with conflicting results regarding the prognostic and predictive value of PD-L1 as a biomarker in breast cancer [26]. While some studies suggest the association between PD-L1 expression and negative prognostic parameters (such as tumor size, higher grade and proliferative activity, absence of steroid receptor expression) [25, 27–30] in some studies a highly significant association between PD-L1 expression and a high density of TILs (as an independent favorable prognostic factor) was shown [23, 24, 31, 32]. Finally, the predictive value of PD-L1 expression in the selection of candidates for immune checkpoint inhibitor therapy, even within the TNBC subtype, has been questioned by some recent studies [26, 33].

Therefore, numerous authors share the opinion that it is necessary to optimize the use of PD-L1 as a biomarker in breast cancer [22, 26, 34] and that the analysis of its expression should be placed in the context of the density and composition of sTILs [22, 26, 34, 35]. Despite the complexity of anti-tumor immune responses, the presence of stromal TILs is considered to be a robust prognostic and predictive biomarker in breast cancer [36] and guidelines for its routine scoring have been provided by the International TILs Working group [37]. According to these, sTILs should be scored as a continuous variable (the mean percentage of tumor stroma covered by mononuclear cells), although clinically significant cut-off value of sTILs density still remains unknown [37].

In addition, as the focus of researchers has so far been almost exclusively placed on locally advanced and metastatic TNBC, data on PD-L1 expression and characteristics of intratumoral inflammatory infiltrate in other molecular subtypes, especially in early breast cancer, are still insufficient in the literature [25].

Therefore, the aim of this study is to examine the relationship between the density and composition of stromal TILs and the characteristics of peritumoral lymphoid aggregates and PD-L1 expression in dif-

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ferent molecular subtypes of early breast cancer and determine the threshold value percentage of sTILs at which PD-L1 positivity can be predicted in early breast cancer.

Material and methods

Patients. The study included all female patients who were diagnosed with stage IA-IIIA invasive breast cancer (according to the eighth edition of the TNM classification [38]) on surgically obtained material at the Center for Pathology of the Clinical Center of Montenegro, Montenegro, between 2016 and 2020 and which did not previously receive neoadjuvant therapy. The study was conducted according to the ethical principles governing medical research and human subjects as laid down in the Helsinki Declaration and approved by the Ethical Committee of the Medical Faculty of the University of Montenegro (approval number 1492/2, dated 23.09.2022).

Based on the existing pathomorphological reports with data on the degree of immunohistochemical (IHC) expression of steroid hormone receptors (ER — estrogen and PR — progesterone receptors), human epidermal growth factor receptor 2 (HER-2) status and Ki67 proliferation index value, according to St. Gallen consensus [39], the samples were classified into five groups with the following molecular subtypes: Luminal A, Luminal B HER-2 positive, Luminal B HER-2 negative, non-luminal HER-2 positive and TNBC.

ER and PR were considered positive if the Allred score was ≥ 3, while the presence of HER-2 overexpression was assessed according to current ASCO/CAP (American Society of Clinical Oncology/College of American Pathologists) guidelines [40] on immunohistochemically stained sections and sections stained by DDISH (Dual-color dual-hapten *in situ* hybridization) method in the case of an equivocal result of the previously conducted IHC analysis.

Finally, 95 samples (19 from each of the five molecular subtypes) which contained enough material in the available archived paraffin blocks for the planned further immunohistochemical analysis were selected, whereby we standardized the sample in relation to age, so that the average age of the subjects was very similar in each of the five investigated groups. The mean age of study participants was 59.68 ± 11.71 (mean ± SD) years.

Analysis of HE stained histological sections from original surgical specimens. By examining archived microscopic slides, stained with the standard hematoxylin-eosin (HE) method, the histological type and grade of the tumor was confirmed. The density of sTILs was scored as a continuous variable according to the International TIL Working group recommendations, that is: all mononuclear immune cells were taken into account and polymorphonuclear granulocytes were excluded based on morphology [37].

In addition, the density of sTILs was also recorded semiquantitatively, using the methodology suggested by Cimino-Mathews *et al.*, as mild (< 5% of the tumor stroma), moderate (focal infiltrate in 5–50% of the tumor stroma) and diffuse (diffuse infiltrate in ≥ 50% of the tumor stroma) [22] (Fig. 1).

Finally, presence of peritumoral lymphoid aggregates (PLA) was recorded and scored using the same methodology [22] as absent, focal (rare isolated clusters of lymphocytes), moderate (multiple lymphoid aggregates) and highly developed (multiple lymphoid aggregates with well-developed germinal centers) (Fig. 2).

Tissue microarray (TMA) preparation, immunohistochemical staining and analysis. In selected samples, two TMAs measuring 3 mm were formed from the archived paraffin blocks for each patient using the Quick Ray Manual Tissue Microarrayer set (Untima Co., Ltd., Gyeonggi-do, South Korea). The obtained preparations were first stained with the standard HE technique, in order to confirm the adequacy of the sample and facilitate orientation during the interpretation of immunohistochemically stained sections.

For the purpose of antigen retrieval, TMAs were treated in 10 mM citrate buffer, pH 6.0, in microwave oven for 10 min, and then washed out with deionized water. Endogenous peroxidase was blocked using a 3% hydrogen peroxide solution at room temperature for 10 min. The sections were than incubated with

Figure 1. Semiquantitative stromal tumor-infiltrating lymphocytes (sTILs) density scoring was applied to the early breast cancer tumors: **A.** Mild stromal infiltrate (a small number of mononuclear cells is seen in an area that comprises < 5% of the tumor stroma). **B.** Moderate (focal) stromal infiltrate (clusters of mononuclear cells are covering around 15% of the tumor stroma). **C.** Diffuse stromal infiltrate is completely covering the tumor stroma. Hematoxylin-eosin (HE) staining, magnification: 100×. The sTILs scoring was determined as described in Methods.

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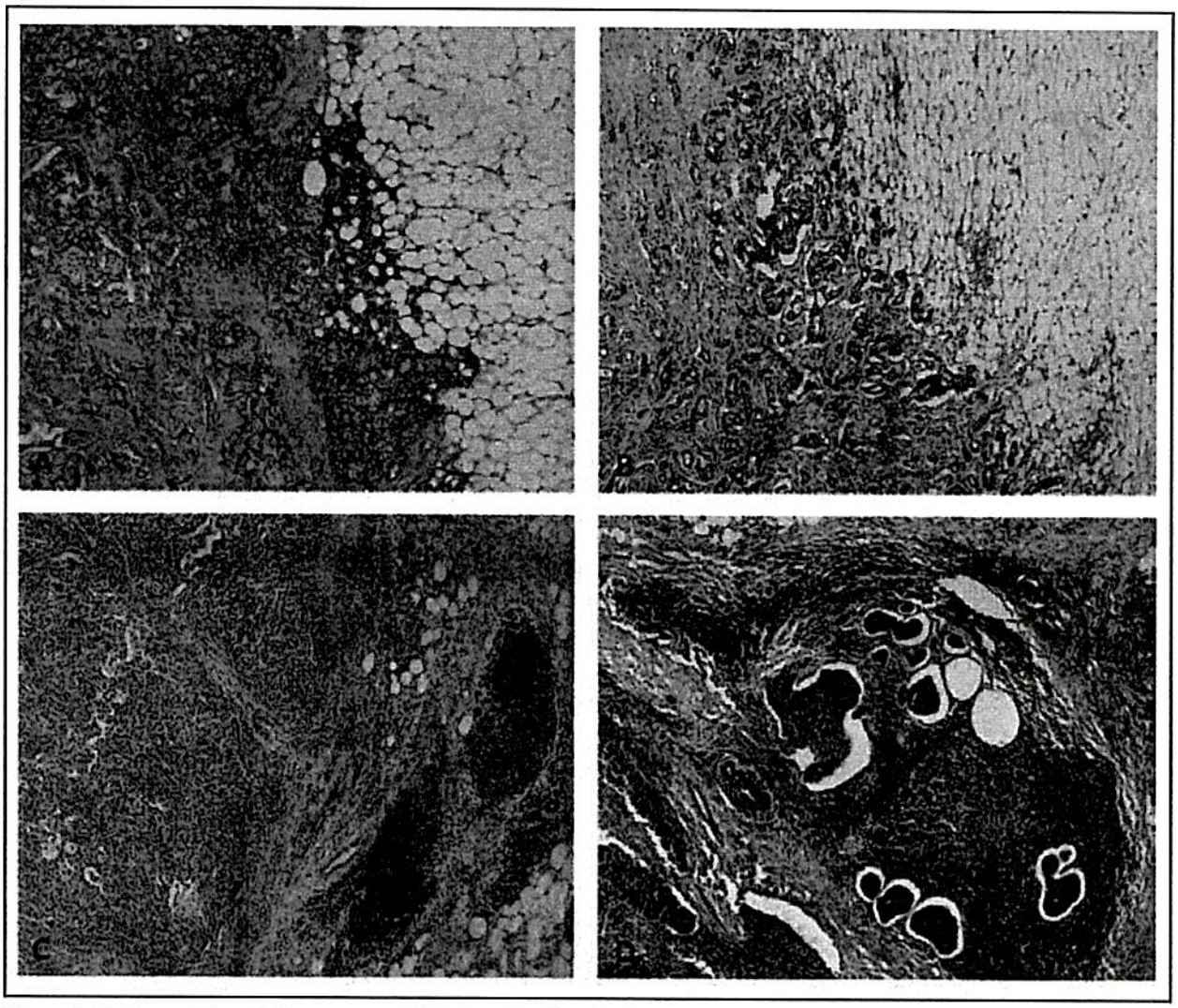

Figure 2. Peritumoral lymphoid aggregates (PLAs) scoring/classification in early breast cancer tumors: **A.** PLAs absent. **B.** Focal PLAs presence (rare isolated clusters of lymphocytes are seen at the invasive front of the tumor). **C.** Moderate PLAs distribution (multiple lymphoid aggregates are present at the tumor border). **D.** Highly developed PLAs (multiple lymphoid aggregates with well-developed germinal centers at the invasive front of the tumor). HE staining, magnification: 40×.

the primary antibody in a moist chamber, at room temperature, for 1 h. The streptavidin-biotin-peroxidase technique was used for antigen visualization according to the standard LSAB+ procedure (DAKO, Carpinteria, CA, USA and Glostrup, Denmark). After each incubation, sections were washed out with Tris-buffered saline solution (TBS, 0.05 M, pH 7.6). The following primary antibodies were used: CD4 (Monoclonal Mouse Anti-Human CD4, Clone 4B12 FLEX Ready to use DAKO, 1:100) and CD8 (Monoclonal Mouse Anti-Human CD8, T-cell, Clone C8/144B FLEX Ready to use DAKO, 1:100).

IHC staining for PD-L1 was performed using PD-L1 (Monoclonal Rabbit Anti-Human PD-L1, Clone SP142, Roche/Ventana Medical Systems, Tucson, AZ, USA) antibody on the Ventana Benchmark GX (Ventana Medical Systems, Tucson, AZ, USA) automated platform, according to the manufacturer's instructions.

Palatine tonsil was used as an external positive control for immunohistochemical staining.

Zeiss Axiolab 5 microscope (Carl Zeiss Microscopy GmbH, Jena, Germany) with the field diameter of 0,65 mm, was used for morphological analysis, where one high power field (HPF, 400×), corresponded to field area of 0.332 mm^2.

For both CD4 and CD8 markers, strong membrane positivity was interpreted as positive result. Quantification of CD4 and CD8 positive sTILs was performed manually by counting positive cells on 9 HPFs what corresponded to 3 mm^2 *per* TMA (that is 18 HPFs, corresponding to 6 mm^2 *per* patient) and the obtained values were expressed as the average number of cells/mm^2/patient. The values were used to calculate the CD4/CD8 ratio.

While assessing PD-L1 expression in immune cells, all the cells showing partial/complete membrane/cytoplasmic staining

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of any intensity were taken into account and the immune cell score (ICS) algorithm was used for scoring [35]. The final result was the mean ICS value, obtained by evaluating both TMAs of each individual patient's tumor. According to the currently valid protocol for evaluating PD-L1 expression in TNBC, an ICS ≥ 1% was considered a positive finding [35].

Statistical analysis. The data were analyzed using IBM SPSS Statistics version 23.0 software (IBM SPSS for Windows, Armonk, NY, USA). Statistical hypotheses were tested using non-parametric statistical tests (Fisher's exact test and Mann-Whitney U test), and the correlation between parameters was described with the help of Phi correlation coefficient. Statistical "ROC" curves and the formula for calculating Youden's index (J = sensitivity + specificity – 1) were used to display the cut-off value of sTILs percentage that predicts PD-L1 positivity. For all the statistical analyses, the level of significance was 0.05.

Results

Qualitative study

All of the three analyzed markers (CD4, CD8 and PD-L1) demonstrated their expected immunohistochemical staining patterns.

As seen in Fig. 3, strong CD4 membranous staining was seen in T-lymphocytes of the interfollicular area of the control tonsillar tissue, along with moderate positivity of germinal center macrophages and absent reaction in squamous epithelium. In breast cancer strong CD4 immunoreactivity (Ir) was seen in stromal T-lymphocytes, with a few positive intratumoral T-lymphocytes located between cancer cells, which were omitted from further analysis.

The CD8 immunohistochemical staining of the tonsillar tissue showed strong membranous reaction, primarily in T-lymphocytes of the interfollicular area, with a few positive intraepithelial T-lymphocytes and absent reaction in squamous epithelium of the tonsil. In breast cancer, strong positivity in stromal T-lymphocytes, with a few positive intratumoral T-lymphocytes (which were not considered in further analysis) was noted (Fig. 4).

Staining pattern and interpretation of PD-L1 immunoreactivity are shown in Fig. 5. In control tissue (tonsil), moderate to strong cytoplasmic/membranous staining was noted in lymphocytes and macrophages in germinal centers, while superficial squamous epithelium remained negative. In PD-L1 positive breast tumors, immunoreactivity was usually seen in clusters of immune cells within the tumor stroma (ICS ≥ 1%), whereas PD-L1 negative tumors showed either no IHC reaction, or positive reaction that was noted only in a few individual cells within the tumor stroma (ICS < 1%).

Quantitative analysis

Out of 95 early breast cancer samples included in the study, positive PD-L1 expression was found in 20 cases (21.5%). Statistical analysis found no significant association between PD-L1 expression and tumor size (U = 717.00; P = 0.76), pT (Fisher exact test = 1.92; P = 0.37), or the pN stage of the disease (Fisher exact test = 0.52; P = 0.93), as well as the molecular subtype of the tumor (Fisher's exact test = 8.25; P = 0.07).
On the other hand, we found a significant connection between PD-L1 expression and the histological grade of the tumor (Fisher exact test = 12.81; P = 0.003),

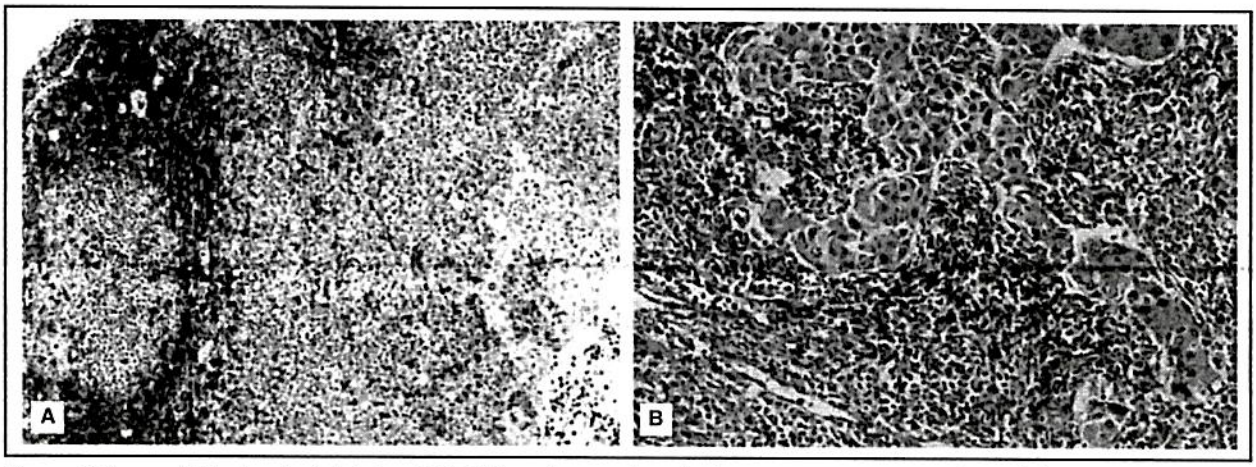

Figure 3. Immunohistochemical staining of CD4+ lymphocytes in early breast cancer tumors. **A.** Control tissue (palatine tonsil) — strong membranous staining is seen in T-lymphocytes of the interfollicular area, along with moderate positivity in the germinal center macrophages and absent reaction in squamous epithelium. IHC, magnification: 40×; **B.** Tumor-infiltrating lymphocytes in breast cancer tissue — strong immunoreactivity is present in stromal T-lymphocytes, with a few positive intratumoral T-lymphocytes located between cancer cells. Immunohistochemistry (IHC), magnification: 100×. Tissue microarrays of 95 breast cancer patients were processed for IHC as described in Methods.

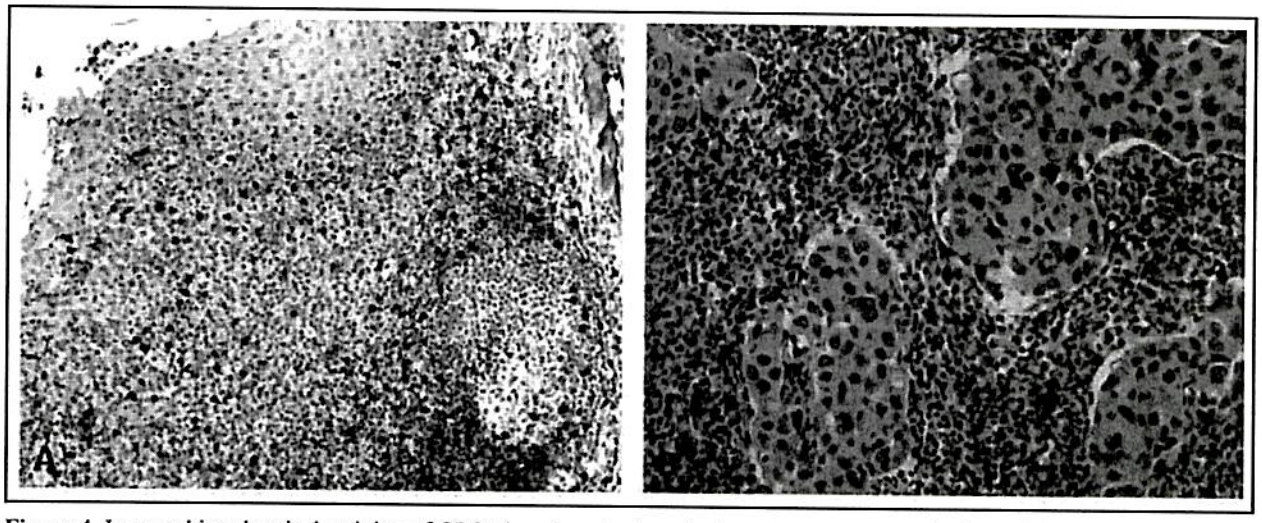

Figure 4. Immunohistochemical staining of CD8+ lymphocytes in early breast cancer tumors. **A.** Control tissue (palatine tonsil) — strong membranous reaction is seen primarily in T-lymphocytes of the interfollicular area, with a few positive intraepithelial T-lymphocytes and absent reaction in squamous epithelium. Immunohistochemistry (IHC), magnification: 40×. **B.** Breast cancer tumor-infiltrating lymphocytes: strong immunoreactivity is seen in stromal T-lymphocytes, with a few positive intratumoral T-lymphocytes. IHC, magnification: 100×. Tissue microarrays of 95 breast cancer patients were processed for IHC as described in Methods.

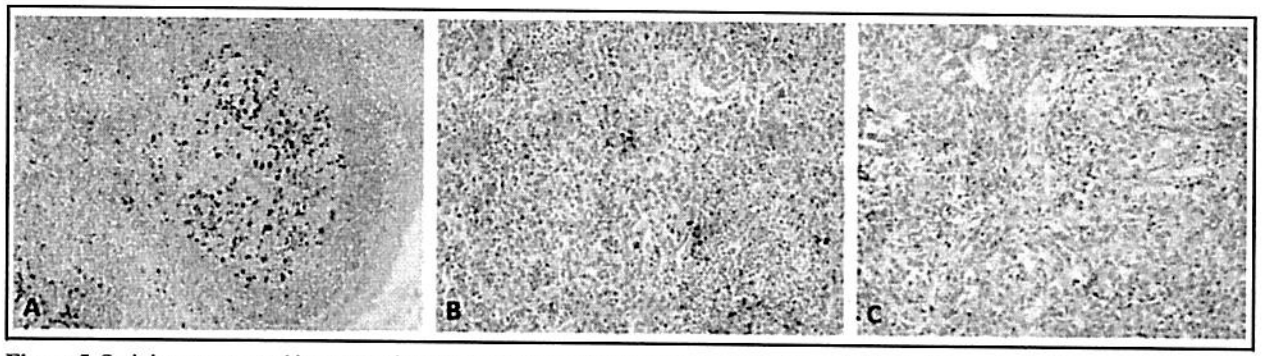

Figure 5. Staining pattern and interpretation of PD-L1 immunohistochemical stainings. A. Control tissue (palatine tonsil) - moderate to strong cytoplasmic/membranous staining is seen in lymphocytes and macrophages in germinal centers, while superficial squamous epithelium remains negative. IHC, Magnification: 40×. B. Breast cancer tumor with positive PD-L1 expression. Immunoreactivity is seen in clusters of immune cells within the tumor stroma (ICS ≥ 1%). IHC, magnification: 100×; C) Breast cancer tumor with negative PD-L1 expression - positive reaction is noted only in a few individual cells within the tumor stroma (ICS < 1%). IHC, magnification: 100×. Tissue microarrays of 95 breast cancer patients were processed for immunohistochemistry and ICS was determined as described in Methods. Abbreviations: ICS — immune cell score; PD-L1 — Programmed cell death receptor ligand 1.

with a moderate positive correlation between these two parameters (Phi = 0.38; P = 0.003). The Z test showed that positive PD-L1 expression occurs statistically significantly more often in patients diagnosed with grade G3 breast cancer, compared to patients diagnosed with grade G1 and G2.

Also, a statistically significantly higher value of the Ki67 proliferative index was determined in patients with positive PD-L1 expression (48.50 ± 21.527; mean ± SD), compared to those without the expression of this marker (33.07 ± 23.980; mean ± SD), (U = 437.00; P = 0.006).

The analysis of parameters related to the antitumor immune response, a strong positive correlation between PD-L1 expression and type of sTIL was found (Phi = 0,88; P < 0,001), and the Z test showed that positive PD-L1 expression was statistically significantly more frequent in tumors with diffuse, compared to moderate and mild types of stromal TILs, regardless of the molecular subtype.

Furthermore, it was determined that the absolute number of both CD4– (U = 61.50; P < 0.001) and CD8– (U = 90.50; P < 0.001) lymphocytes *per* mm² in the tumor stroma was statistically significantly higher in tumors with positive PD-L1 expression (Fig. 6), although no significant predominance of a certain lymphocyte subpopulation was found, that is CD4/CD8 ratio did not differ from the tumors in which PD-L1 expression was absent or present (Fisher exact test = 0.851; P = 0.42).

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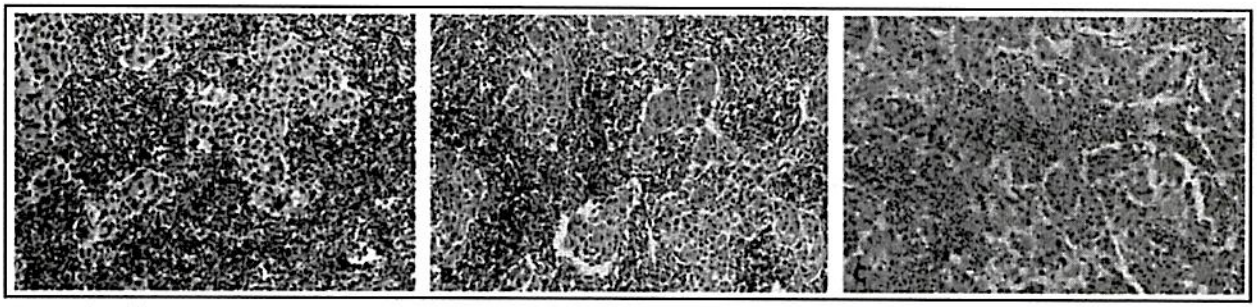

Figure 6. Diffuse stromal mononuclear immune cell infiltrates, with high absolute numbers of (**A**) CD8 lymphocytes, and (**B**) CD4 lymphocytes, that were detected in (**C**) PD-L1 positive breast cancer tumor. IHC, magnification: 100×.

In addition to the type of sTIL, statistically significant difference was found between tumors with positive and negative PD-L1 expression in relation to the characteristics of peritumoral lymphoid aggregates (Fisher's exact test = 12.87; P = 0.003). The correlation coefficient revealed a moderate positive correlation between PD-L1 expression and the type of peritumoral lymphoid aggregate (Phi = 0.37; P = 0.003), and the Z test showed that moderate peritumoral lymphoid aggregates were noted statistically significantly more often compared to focal and absent lymphoid aggregates in tumors with positive PD-L1 expression. No difference was found between the presence of highly-developed lymphoid aggregates in relation to other types of peritumoral lymphoid aggregates in patients with positive PD-L1 expression in breast cancer tumors. However, these observations were not related to tumor molecular subtype.

The results of the association between PD-L1 expression and clinico-pathological features and anti-tumor immune response markers are summarized in Table 1 for discrete variables and Table 2 for continuous variables.

In further analysis, Mann-Whitney test showed a statistically significant difference between the mean value of sTIL density, expressed as the percentage of

Table 1. PD-L1 expression in relation to clinico-pathological characteristics (histological grade, molecular subtype, pT and pN stage of the disease) and anti-tumor immune response markers (density of sTILs and peritumoral lymphoid aggregates and CD4/CD8 ratio) in 95 examined samples of breast cancer (discrete variables)

		PD-L1		Total	P
		Negative	Positive		
Histological grade	G1 (well differentiated) G2 (moderately differentiated) G3 (poorly differentiated)	4 (4.2%) 49 (51.5%) 22 (23.2%)	0 (0%) 5 (5.3%) 15 (15.8%)	4 (4.2%) 54 (56.8%) 37 (39.0%)	0.003
Molecular subtype	Non-luminal HER2+ TNBC Luminal B HER2+ Luminal B HER2- Luminal A	14 (14.7%) 11 (11.6%) 16 (16.8%) 16 (16.8%) 18 (18.9%)	5 (5.3%) 8 (8.4%) 3 (3.2%) 3 (3.2%) 1 (1.1%)	19 (20.0%) 19 (20.0%) 19 (20.0%) 19 (20.0%) 19 (20.0%)	0.07
pT stadium	T1 T2 T3	35 (36.8%) 37 (38.9%) 3 (3.2%)	7 (7.4%) 11 (11.6%) 2 (2.1%)	42 (44.2%) 48 (50.5%) 5 (5.3%)	0.37
pN stadium	N0 N1 N2	52 (54.7%) 11 (11.6%) 12 (12.6%)	13 (13.7%) 4 (4.2%) 3 (3.2%)	65 (68.4%) 15 (15.8%) 15 (15.8%)	0.93
Density of sTILs	Mild Moderate Diffuse	22 (23.2%) 50 (52.6%) 3 (3.1%)	0 (0%) 1 (1.1%) 19 (20.0%)	22 (23.2%) 51 (53.7%) 22 (23.1%)	< 0.001
Peritumoral lymphoid aggregates	Absent Focal Moderate Well developed	7 (7.4%) 27 (28.4%) 37 (38.9%) 4 (4.2%)	0 (0%) 1 (1.1%) 15 (15.8%) 4 (4.2%)	7 (7.4%) 28 (29.5%) 52 (54.7%) 8 (8.4%)	0.003
CD4/CD8 ratio	CD4/CD8 < 1 CD4/CD8 > 1	22 (23.2%) 53 (55.8%)	8 (8.4%) 12 (12.6%)	30 (31.6%) 65 (68.4%)	0.42

Abbreviations: PD-L1 — Programmed death receptor ligand 1; sTils — stromal tumor-infiltrating lymphocytes.

Table 2. PD-L1 expression in relation to the density of sTILs expressed as a continuous variable, area density of CD4 and CD8 lymphocytes and Ki67

	PD-L1	Mean value ($\bar{x} \pm SD$)	P
sTILs (%)	Negative Positive	15.31 ± 14.32 68.75 ± 16.85*	< 0.001
CD4 (*per* mm²)	Negative Positive	31.65 ± 30.18 175.25 ± 87.62*	< 0.001
CD8 (*per* mm²)	Negative Positive	28.16 ± 33.79 150.60 ± 78.19*	< 0.001
Ki67 (%)	Negative Positive	33.07 ± 23.980 48.50 ± 21.527*	0.006

Abbreviations as in the legend to Table 1.

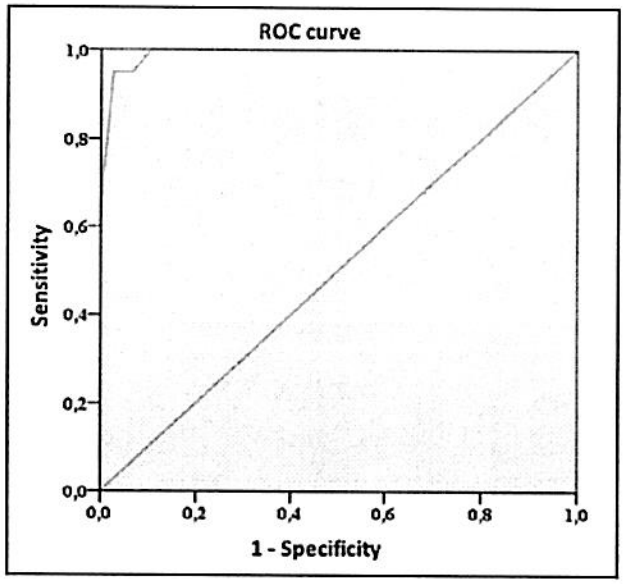

Figure 7. ROC curve for predicting PD-L1 positivity based on the density of stromal tumor-infiltrating lymphocytes. The curve was constructed by plotting the true positive rate (the proportion of observations that were correctly predicted to be positive) against the false positive rate (the proportion of observations that were incorrectly predicted to be positive out of all negative observations). The area under the ROC curve for assessing the positivity of PD-L1 expression based on the density of stromal tumor-infiltrating lymphocytes speaks in favor of excellent diagnostic accuracy (AUC = 0.992; P < 0.001). Abbreviations: AUC — area under the curve; ROC — receiver operating characteristic.

tumor stroma covered by lymphocytes, between breast cancers with positive and negative PD-L1 expression (U = 12,50; P < 0.001). The area under the ROC curve for assessing the positivity of PD-L1 expression based on the density of sTILs speaks in favor of excellent diagnostic accuracy (AUC = 0,992; P < 0.001), and based on the highest value of Youden's index (Youden's index = 0.923), a cut-off value of 53% was established (Fig. 7).

Discussion

To date, a large number of studies with conflicting results in terms of clinical, prognostic and predictive significance of the presence of PD-L1 expression in breast cancer has been published [25, 26, 28, 31–34, 41, 42]. On the other hand, we are witnessing that the development and clinical application of targeted therapy in the form of PD-1/PD-L1 inhibitors is progressing at a much faster pace compared to basic mechanistic studies and the understanding of all aspects of PD-1/PD-L1-mediated signaling [43]. Therefore, the need to take a few steps back in order to optimize the routine use of PD-L1 as a biomarker in breast cancer has increasingly been appreciated.

However, one must take into account the problematic comparability of the results published so far, which is primarily due to the application of different methodologies for the evaluation of PD-L1 expression. While some authors used molecular techniques for these purposes, most used immunohistochemistry, while applying a wide range of different antibodies and different scoring systems (including the assessment of PD-L1 expression in different cell populations), as well as very different threshold values at which the expression is of this marker was considered positive [34].

In our study, apart from the strict criteria for the inclusion of patients and tumor samples (treatment naive, surgically obtained specimens of early breast cancer, age standardized groups), PD-L1 expression was determined using Ventana PD-L1 (SP142) immunohistochemical assay and interpreted according to the official accompanying guide (designed and approved as companion diagnostic test to evaluate the clinical benefit from the use of atezolizumab in locally advanced and metastatic TNBC) [44], all of which we consider to be advantages in terms of obtaining relevant results.

Analyzing PD-L1 expression in immune cells of the tumor microenvironment of different molecular subtypes of early breast cancer in our study, we determined positive PD-L1 expression in 21.5% of cases, which is comparable to the results published by Muenst *et al.* who reported PD-L1 expression in 23% of 650 breast cancer samples [28] and Sabatier *et al.* who found PD-L1 upregulation in 20% of 5,454 samples of breast cancer [29].

Higher frequency of PD-L1 positivity was reported by Ghebeh *et al.* [27] who found PD-L1 expression in 50% of 44 analyzed breast cancers samples, while Mittendorf *et al.* reported a lower percentage of PD-L1 positive tumors (19% positive cases in their sample of 105 TNBC cases, compared to 42.1% positive TNBC tumors in our study). Although these

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authors also used immunohistochemistry, the variations in frequency of positive PD-L1 expression may be attributed to the differences in the experimental design, as they used a different primary antibody and scoring system, along with a very different cut-off values for PD-L1 positivity.

The highest percentage of PD-L1 positive tumors was reported by mRNA expression studies. For example, Schalper *et al.* reported PD-L1 expression in 58% of breast cancer specimens [45]. However, higher frequency of PD-L1 expression in these studies might be explained by the fact that mRNA expression may not always correlate with actual protein expression [28].

Similar to the results published by other authors [25, 29], we found a statistically significant association between PD-L1 expression and poor prognostic factors, such as histological grade and tumor mitotic index, but not tumor size and the stage of disease, which could be explained by the fact that present study was performed in early breast cancer cases.

Also, we observed a statistically significant association between PD-L1 expression and the density of sTILs, which is in accordance with previously published results [22, 25, 31]. To our best knowledge, we could present for the first time, the cut-off value of the percentage of sTIL (53%) at which PD-L1 positivity can be predicted with excellent accuracy in early breast cancer tumors.

Although current literature lacks sufficient data on the dynamic changes in the distribution and quantity of different subpopulations of T cells during breast cancer progression, it has been suggested that CD4 and CD8 T-lymphocytes might have opposing roles in breast cancer progression and outcome [46]. While most authors agree that CD8 lymphocytes represent a key cell population that controls the effectiveness of the antitumor immune responses in general [5, 45, 47], the role of CD4 lymphocytes, and their subtypes, in the antitumor response and tumor progression is much more complex and dynamic [5]. For example, Huang *et al.* showed that in early lesions of breast cancer, Th1 cells represented the dominant subpopulation of CD4 lymphocytes in the stromal infiltrate and that the increase in the number of CD4 cells, with the predominance of FoxP3 regulatory and Th17 subpopulations of T-lymphocytes, was associated with the progression of the disease [46]. The same authors demonstrated a positive correlation between the number of CD4 T-lymphocytes in the stromal infiltrate and the advanced stage of the disease.

Similar to the results of previously conducted research, our study showed higher number of CD8 T-lymphocytes in the stromal infiltrate of PD-L1 positive compared to PD-L1 negative tumors [29, 48], although in our study the same observation was made for CD4 lymphocytes. However, we did not find a statistically significant predominance of one subpopulation of T-lymphocytes over the other (CD4 *vs.* CD8 cells) in PD-L1 positive *vs.* PD-L1 negative tumors. This could be a consequence of selecting patients with early breast cancer as a studied cohort, since it was demonstrated that with disease progression CD4 T-lymphocytes infiltrate the tumor more rapidly compared to CD8 T-lymphocytes, which makes them a predominant lymphocyte population in late breast cancer [46].

Considering the dynamic changes in the composition of the intratumoral lymphocytic infiltrate (predominantly within the population of CD4 T-lymphocytes) during the development of malignant breast tumors, in future research it would be interesting to analyze the expression of certain subpopulations of CD4 lymphocytes, especially FoxP3-positive regulatory T-lymphocytes, whose presence is considered the main obstacle in achieving effective antitumor immunity and good response to immunotherapy [46].

In addition to sTILs, we also analyzed the association between PD-L1 expression and presence and characteristics of peritumoral lymphoid aggregates and found that PD-L1 positivity occurs significantly more often in tumors with a higher density of peritumoral infiltrates. This has been previously reported by Cimino-Mathews *et al.*, who identified presence of peritumoral lymphoid aggregates in 59% of PD-L1 positive breast cancer cases [22].

Peritumoral lymphoid aggregates, also termed tertiary lymphoid structures (TLS), have emerged as another biomarker of active antitumor immune response [22]. Apart from T-lymphocytes, these structures are known to contain a significant number of B-lymphocytes [22], whose role in this process has been intensively investigated recently. Generally, presence of TLS at the border between the tumor and the surrounding tissue was found to be associated with a good prognosis and favorable response to immune checkpoint inhibitor therapy, even in tumors with a low mutational burden [49]. When it comes to studies on breast cancer, the presence of TLS was found to be associated with a favorable prognosis [22, 50–52]. Although the available literature lacks studies that analyzed the presence of B-lymphocytes in peritumoral lymphoid aggregates in the context of PD-L1 expression, we believe that this should become subject of future studies.

Contrary to the results published so far, in which the presence of PD-L1 expression has been dominantly associated with TNBC [25, 26, 31, 53, 54] in our study this association did not reach statistical significance

(P = 0.07), although the highest percentage of PD-L1 positive tumors belonged to this molecular subtype of breast cancer. The discrepancy between our result and the results of these studies is probably due to the relatively small size of our sample. However, since it has been demonstrated that tumor immunogenicity in breast cancer decreases with progression of the disease [55], this difference might also be due to the fact that present study was performed in early stages of breast cancer, where increased sTILs may occur more often across other (non-TNBC) molecular subtypes [56].

In conclusion, our results indicate that the density of sTILs might be a better predictor of PD-L1 positivity in early breast cancer than the molecular subtype itself. Thus, when assessing a patient's suitability for PD-L1 inhibitor therapy and consequently setting the indication for the evaluation of PD-L1 status in early breast cancer, we believe that all patients whose tumors show a density of sTIL above 53% should be taken into account, regardless of HER2 expression and hormone receptor status.

The higher density of sTILs and peritumoral lymphoid aggregates, as well as the absolute number of CD4 and CD8 lymphocytes in the stromal mononuclear cells' infiltrates in PD-L1 positive tumors suggest that the interpretation of PD-L1 expression should be done exclusively in the context of the density and composition of the intra- and peritumoral lymphoid infiltrates. In order to optimize the use of PD-L1 as a biomarker in breast cancer, studies on larger samples are necessary to improve our understanding of the dominant subpopulations of T and B lymphocytes in PD-L1 positive cancers and define their associations with the course of the disease and patient survival.

Article information and declarations

Data availability statement

The data that support the findings of this study are not openly available due to sensitivity and patient privacy protection, but are available from the corresponding author upon reasonable request. Data are located in controlled access data storage at the Clinical center of Montenegro.

Ethics statement

The study was conducted according to the ethical principles governing medical research and human subjects as laid down in the Helsinki Declaration and approved by the Ethical Committee of the Medical faculty of the University of Montenegro.

Author contributions

All authors contributed to the study design and write up of the manuscript. JV collected the sample, performed the microscopic evaluation and statistical analysis of obtained data.

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Conflict of interest

All authors declare that they have no conflicts of interest.

Supplementary material

All the materials, including tables and figures, will be provided within the manuscript, as a single document.

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BIOGRAFIJA KANDIDATA

Jelena Vučinić rođena je 11. 6. 1989. godine u Nikšiću, gdje je završila osnovnu školu, gimnaziju i nižu muzičku školu kao nosilac diplome „Luča".

Osnovne studije na Medicinskom fakultetu u Podgorici (studijski program Medicina) završila je 2014. godine u predviđenom roku, sa prosječnom ocjenom 9,71. Tokom osnovnih studija u dva navrata boravila je na univerzitetskim klinikama u Krakovu i Istanbulu, gdje je sticala radno iskustvo u okviru programa razmjene studenata.

Radni odnos zasnovala je 2015. godine u Centru za patologiju Kliničkog Centra Crne Gore, gdje danas radi kao specijalista patološke anatomije, a specijalističke studije završila je 2020.godine na Medicinskom fakultetu Univerziteta u Novom Sadu.

Magistarske studije iz oblasti biomedicinskih nauka (ćelijske patologije) završila je na Univerzitetu Vestminster u Londonu 2017. godine kao njegov puni stipendista, a u okviru svojih istraživanja bavila se patologijom i genomikom karcinoma dojke.

Od 2017. do 2024. godine bila je radno angažovana kao saradnik u nastavi na Katedri za histologiju i embriologiju Medicinskog fakulteta u Podgorici.

Za vrijeme svog radnog angažmana aktivno se bavila naučno-istraživačkim radom iz oblasti patologije, a autor je i koautor brojnih naučnih radova koji su prikazani na stručnim kongresima i objavljeni u naučnim časopisima koji se citiraju u međunarodnim bazama.

U periodu od 2018.do 2020. godine bila je jedan od učesnika nacionalnog projekta naučne i tehnološke saradnje Crne Gore i Italije.

Doktorske studije upisala je 2019. godine na Medicinskom fakultetu u Podgorici, a polazna istraživanja odbranila 12. 1. 2021. godine.

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Naučni radovi koji se citiraju u međunarodnim bazama:

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Vučković Lj, Vučinić J, Raonić J. Histologija i embriologija – praktikum. 2019. Univerzitet Crne Gore, Medicinski fakultet u Podgorici.

Naučni radovi prezentovani na kongresima:

- **Vučinić J**, Raonić J, Vučković Lj, Vukmirović F, Golubović M, Nenezić T, Kavarić P. Metastaza u gornjem urinarnom traktu kao inicijalna prezentacija invazivnog lobularnog karcinoma dojke. XXVI Nacionalni kongres UPCS, Zlatibor, Srbija, 18.-19.4.2018. Materia Medica 2018;34(1):65-6;

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- **Vucinic J**, Radojevic N, Cukic D. Toxicological Findings in Choking in Adult Psychiatry Patients. Proceeding od the LXIX Annual Meeting of the American Academy of Forensic Science; 2017 February 13-18; New Orleans, USA.

- Vučković Lj, Raonić J, Vukmirović F, Golubović M, Nenezić T, Ćulafić T, Miladinović M, **Vučinić J**. Immunohistochemical determination of breast cancer molecular subtypes in the Clinical center of Montenegro. 29th European Congress of Pathology, Amsterdam, Netherlands, 2.-6-9-2017. Virchow Archiv;471(1):S67.

- **Vučinić J**, Vučković Lj, Zvrko E. Metastaza karcinoma dojke u pljuvačnoj žlijezdi – prikaz slučaja. XV kongres ljekara Crne Gore sa međunarodnim učešćem. Bečići, 21-25.10.2015. Medicinski zapisi (Medical esseys) 2015;64(1):216;

UNIVERZITET CRNE GORE

MEDICINSKI FAKULTET

Na osnovu odluke Senata Univerziteta Crne Gore br. 03-4137/1 od 15.10.2020. godine, imenovana sam za mentora za izradu doktorske disertacije kandidatkinje mr sci. med. Jelene Vučinić. U fazi predaje doktorske disertacije na pregled i ocjenu, u skladu sa Pravilima doktorskih studija Univerziteta Crne Gore dajem:

SAGLASNOST

Saglasna sam da kandidat mr sci. med. Jelena Vučinić može predati doktorsku disertaciju pod nazivom „Medusobna korelacija gustine tumor-infiltrišućih limfocita, CD4 i CD8 pozitivnih limfocita i PD-L1 ekspresije i njihova korelacija sa patološkim prognostičkim parametrima u molekularnim podtipovima ranog karcinoma dojke " na pregled i ocjenu.

S poštovanjem,

Ljiljana Vučković

U Podgorici 25.4.2024. god.

Prof. dr Ljiljana Vučković

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Datum / Date 19. 04 2019

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 i 3/19) i člana 32 stav 1 tačka 9 Statuta Univerziteta Crne Gore, Senat Univerziteta Crne Gore, na sjednici održanoj 19. aprila 2019.godine, donio je

O D L U K U
O IZBORU U ZVANJE

Dr FILIP VUKMIROVIĆ bira se u akademsko zvanje **redovni profesor Univerziteta Crne Gore za oblast Patologija iz Dijagnostičke grupe bazičnih medicinskih predmeta** (Patološka anatomija, osnovne studije, studijski program **Medicina, Opšta patologija**, osnovne studije, studijski program **Stomatologija i Oralna patologija**, osnovne studije, studijski program Stomatologija) **na Medicinskom fakultetu Univerziteta Crne Gore**, na neodređeno vrijeme.

SENAT UNIVERZITETA CRNE GORE
PREDSJEDNIK

Prof.dr Danilo Nikolić, rektor

BIOGRAFIJA

Ime i prezime: Filip Vukmirović

Prof. dr Filip Vukmirović rođen je 18.12.1974. godine na Cetinju.

Osnovnu i srednju školu završio je na Cetinju i dobitnik je diplome Luča.

Medicinski fakultet u Prištini upisao je 1993. godine i isti završio 1999. godine. Tokom studiranja bavio se naučno-istraživačkim radom i kao autor i koautor više studentskih radova učestvovao na 3 Kongresa studenata medicine i stomatologije. Kao student od 1997. do 1999. godine obavljao je funkciju predsjednika Centra za naučno istraživački rad i saradnju Medicinskog fakulteta u Prištini.

Magistarske studije, smjer onkologija, na Medicinskom fakultetu u Kragujevcu upisao je 1999. godine. Položio je sve predviđene ispite sa prosječnom ocjenom 10,0. Magistarski rad sa temom *«Korelativna kvantitativna analiza značaja vrijednosti humanog epidermalnog faktora rasta receptora 2, sa statusom estrogenskih i progesteronskih receptora kod invazivnog duktalnog karcinoma dojke»* odbranio je 27.06.2003. godine na Medicinskom fakultetu u Kragujevcu.

Specijalizaciju iz Patološke anatomije upisao je 15.10.2001. godine na Medicinskom fakultetu u Novom Sadu i istu završio 26.10.2004. godine sa ocjenom odličan.

Doktorske studije, upisao je 2005. godine na Medicinskom fakultetu u Foči. Doktorsku disertaciju pod nazivom: *„Prognostički značaj analize tumorske angiogeneze, ekspresije vaskularnog endotelnog faktora rasta i epidermalnog faktora rasta receptora u karcinomima želuca"* odbranio je 11.10.2007. godine na Medicinskom fakultetu u Foči, Univerziteta u Istočnom Sarajevu.

Bio je član istraživačkog tima u projektu ***Maligni epitelni tumori oralne sluznice u Crnoj Gori.***

Bio je član istraživačkog tima u projektu ***Cerebrovaskularne bolesti u stanovništvu Crne Gore,*** Projekat Crnogorske akademije nauka i umjetnosti.

Bio je član istraživačkog tima u projektu ***Biološke karakteristike malignoma dojke i njihova povezanost sa matičnim kancerskim ćelijama.*** Nacionalni projekat - Ministratvo nauke i Ministrastvo zdravlja Crne Gore.

Bio je član istraživačkog tima u projektu ***Identifikacija najpouzdanije i najreproducibilnije metode za rutinsko određivanje Ki67 skora kod invazivnog karcinoma dojke.*** Međunarodni bilateralni projekat sa Nacionalnim institutom za tumora Aviano.

Član je istraživačkog tima projekta: ***RECOGNISED*** (HORIZONT 2020).

Član je Udruženja patologa Srbije i Crne Gore i European Society of Pathology.

Bio je član Komisije za kontinuiranu edukaciju Ljekarske komore Crne Gore.

Bio je član Naučnog odbora i Suda časti Univerziteta Crne Gore.

Bio je predsjednik Medicinskog odbora Kliničkog centra Crne Gore.

Rukovodilac je Komisije za doktorske studije Medicinskog fakulteta Univerziteta Crne Gore.

PODACI O RADNIM MJESTIMA I IZBORIMA U ZVANJE

Po završetku fakulteta počeo je sa radom u Domu zdravlja na Cetinju, gdje je obavio obavezni pripravnički staž.

Nakon toga, od 01.09.2000. godine, radni odnos nastavlja na Medicinskom fakultetu u Podgorici kao stručni saradnik na predmetu Patološka anatomija.

Od 2000. godine radni odnos zasniva kao klinički ljekar u Centru za patologiju i sudsku medicinu Kliničkog Centra Crne Gore, dok honorarno obavlja posao stručnog saradnika na predmetu Patološka anatomija na Medicinskom fakultetu u Podgorici. Od završctka magistarske teze u junu 2003. do 2008. godine angažovan je kao saradnik u nastavi na istom predmetu. Za docenta na Medicinskom fakultetu u Podgorici na predmetu Patološka anatomija izabran je 2008. godine. Za vanrednog profesora izabran je 2013. Godine, a za redovnog profesora na predmetu Patološka anatomija izabran je 2019. godine. Od 2013. godine je rukovodilac Komisije za doktorske studije Medicinskog fakulteta Univerziteta Crne Gore.

Po završetku specijalizacije iz Patološke anatomije, 2004. godine, radi kao specijalista patolog u Centru za patologiju i sudsku medicinu Kliničkog Centra Crne Gore, gdje se od novembra 2007. godine nalazi na mjestu načelnika Odjeljenja patologije, a od 2017.g direktora Centra za patologiju.

Od aprila 2009.godine do septembra 2011. Godine, te od 2016 do 2021. godine obavljao je funkciju direktora Centra za nauku Kliničkog centra Crne Gore.

Od 2009. do 2011.godine obavljao je funkciju predsjednika Etičkog komiteta Kliničkog centra Crne Gore i predsjednika Medicinskog odbora Kliničkog Centra Crne Gore.

Od 2022. godine je član Odbora za strateško planiranje razvoja nauke i umjetnosti Univerziteta Crne Gore.

Usavršavanja:

- 2017 – Kasel Njemačka, kurs PD-L1 u karcinomu pluća
- 2015 - ALK Testing Workshop, University Hospital Sanchinarrro, Madrid, Španija.
- 2017 - ALK and ROS1 Testing Technical Training Workshop. Antwerp Univerity Hospital, Antverpen, Belgija, 15.0.2017.
- 2018 PD-L1 Pathology Workshop, Novi Sad

KLASIFIKACIONA BIBLIOGRAFIJA

NAUČNOISTRAŽIVAČKA DJELATNOST

Radovi objavljeni u časopisima koji se nalaze u međunarodnim bazama podataka

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2. **Filip Vukmirovic**, Irena Tomasevic Vukmirovic, Mihailo Vukmirovic. Clinicopathological features of ovarian Brenner tumors in Montenegro. Central European Journa of Medicine. Vol 8, Issue 2, 2013, 146.-148.
3. **Filip Vukmirović**, Irena Tomašević Vukmirović, Mihailo Vukmirović. Von Meyenburg complex (hamartoma of bile dust) mimicking liver metastases. Vojnosanit Pregl 2013; 70(11): 1059-1061. ISSN: 0042-8450.
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5. **Filip Vukmirovic**, Mihailo Vukmirovic, Irena Tomasevic Vukmirovic. Petar Kavaric. Renal lipoma: a case report. Central European Journal of Medicine 8 (3), 328-330.
6. Mihailo Vukmirovic, Irena Tomasevic Vukmirovic, Lazar Angelkov. **Filip Vukmirovic**. Emotional stress as a cause of syncope and *torsade de pointes* in patients with long QT syndrome. Vojnosanit Pregl 2015; 72(2): 192-195. ISSN: 0042-8450.
7. Velimir Miloševic, **Filip Vukmirovic**, Miljan Krstic, Miljan Zindovic, Dragos Stojanovic, Snezana Jancic. Involvement of leptin receptors expression in proliferation and neoangiogenesis in colorectal cancer. JBUON 2015; 20(1): 100-108. ISSN1107-0625.
8. Velimir Miloševic, **Filip Vukmirovic**, Miljan Zindović, Miljan Krstic, Sanja Milenković, Snezana Jancic. Interplay between expression of leptin receptors and mucin histochemical aberrations in colorectal adenocarcinoma. RJME 2015; (56(2 Suppl):709-716. ISSN 1220-0522.
9. Nemanja Radojevic, **Filip Vukmirovic**, Ivana Curović and Miodrag Soc. Asymptomatic syphilitic massive necrosis of the spleen in late syphilis. Int J STD AIDS 2013. Vol 24 (11): 912-915. ISSN: 0956-4624 . DOI:10.1177/0956462413490145.
10. Mihailo Vukmirovic, Aneta Bošković, Zoran Bukumirić, Irena Tomasevic Vukmirovic, **Filip Vukmirovic**. Predictions and outcomes of new-onset atrial fibrillation in patients with acute myocardial infarction. Vojnosanit Pregl 2017; 74(8): 742-748. ISSN: 0042-8450.
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15. Saša Raičević, Kristina Radoman, Saša Radović, Ljiljana Vučković and **Filip Vukmirović**. Fibrothecoma in a virgo intacta adolescent with elevated levels of CA 125 and B-hCG: a case report. Children. 2022;9(6):847. DOI: 10.3390/children9060847.
16. Maša Ždralević, Janja Raonić, Natasa Popovic, Ljiljana Vučković, Isidora Rovčanin Dragović, Batrić Vukčević, Vladimir Todorović. **Filip Vukmirović**, Flaviana Marzano, Apollonia Tullo, Nicoletta Guaragnella, Sergio Giannattasio, Miodrag Radunović. The role of miRNA in colorectal cancer diagnosis: A pilot study. Oncol Lett. 2023 May 4;25(6):267. doi: 10.3892/ol.2023.13853

STRUČNA DJELATNOST

Članstva:

- Naučni odbor Univerziteta Crne Gore
- Sud časti Univerziteta Crne Gore
- Radna grupa za ranu detekciju karcinoma dojke Ministarstva zdravlja Crne Gore
- Ljekarska komora Crne Gore
- Evropsko udruženje patologa
- Udruženja patologa i citologa Srbije
- Komisija za edukaciju Ljekarske komore Crne Gore
- Komisija za evaluaciju Univerziteta Crne Gore
- Odbor za strateško planiranje razvoja nauke i umjetnosti Univerziteta Crne Gore

Projekti (učesnik):

- Član istraživačkog tima u projektu ***Cerebrovaskularne bolesti u stanovništvu Crne Gore,*** Projekat Crnogorske akademije nauka i umjetnosti.
- Član istraživačkog tima u projektu ***Maligni epitelni tumori oralne sluznice u Crnoj***

Gori

- Član istraživačkog tima u projektu ***Biološke karakteristike malignoma dojke i njihova povezanost sa matičnim kancerskim ćelijama.*** Nacionalni projekat - Ministratvo nauke i Ministrastvo zdravlja Crne Gore
- Član istraživačkog tima u projektu ***Identifikacija najpouzdanije i najreproducibilnije metode za rutinsko određivanje Ki67 skora kod invazivnog karcinoma dojke.*** Međunarodni bilateralni projekat sa Nacionalnim institutom za tumora Aviano.
- Član istraživačkog tima projekta: ***RECOGNISED*** (HORIZONT 2020)

Ostalo:

- Recezent rukopisa »Praktikum iz makroskopskog pregleda u patologiji«, urednice Milane Panjković, odlukom Vijeća Medicinskog fakulteta u Novom Sadu, odluka broj 05-14/9-2016/2-4 od 8.6.2018.
- Recenzija udžbenika Patologija, urednika Pavla Budakova i Živke Eri, Medicinski fakultet Novi Sad, 2017.
- Direktor Centra za nauku Kliničkog centra Crne Gore
- Predsjednik medicinskog odbora Kliničkog centra Crne Gore
- Rukovodilac Komisije za doktorske studije Medicinskog fakulteta u Podgorici
- Prodekan za nastavu Medicinskog fakulteta u Podgorici
- Član Sektorske komisije za razvoj kvalifikacija u zdravstvu Ministarstva prosvete Crne Gore
- Član uredničkog odbora (Editorial Board) Endocrine Oncology and Metabolism (ISSN 1849-8922)
- Učesnik ALK Testing Workshop, University Hospital Sanchinarrro, Madrid, Španija 3.jun 2015.
- Učesnik ALK and ROS1 Testing Technical Training Workshop. Antwerp Univerity Hospital, Antverpen, Belgija, 15.0.2017.
- Predavač na III Arome-Montenegro Course „Bridge between Science and Clinics in Oncology, 4-7.10.2017. Budva.
- Učesnik PD-L1 Pathology Workshop, 24.03.2018 Novi Sad
- Učesnik ESMO 2016 Congress, 7-11.10.2016, Copenhagen Danska
- Učesnik XXXI International Congress of the IAP and 28th Congress of the ESP, Cologne, Germany, 25-29 September 2016.
- Predavač Onkološki dani „U korak sa inovacijama“, 01-02.10.2016. Bečići
- Predavač 3 Arome-Montenegro Course, 4-10.10.2017, Budva
- Član Naučnog odbora V Medical konferencije, 31.05-02.06.2018 Budva
- Član Scientific Commitee 16 Naciona SPCA Congress, 18-21.04.2018 Zlatibor
- Član Komisije Ministarstva zdravlja za polaganje stručnih ispita zdravstvenih radnika i zdravstvenih saradnika sa visokim obrazovanjem
- Mentor dijela specijalističkog staža iz Patološke anatomije

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Broj / Ref 03-2603

Datum / Date 23.04 2024.

UNIVERZITET CRNE GORE
MEDICINSKI FAKULTET

Primljeno: 25.04.2024			
Org. jed.	Broj	Prilog	Vrijednost
med	661		

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, 72/19 i 74/20 i 104/21, 86/22, 125/23 i 33/24) i člana 32 stav 1 tačka 9 Statuta Univerziteta Crne Gore, Senat Univerziteta Crne Gore, na sjednici održanoj 23.4.2024. godine, donio je

O D L U K U
O IZBORU U ZVANJE

Dr LJILJANA VUČKOVIĆ bira se u akademsko zvanje **redovni profesor za predmete iz oblasti Morfološka grupa bazičnih medicinskih predmeta na Medicinskom fakultetu Univerziteta Crne Gore,** na neodređeno vrijeme.

SENAT UNIVERZITETA CRNE GORE
PREDSJEDNIK
Prof. dr Vladimir Božović, rektor

BIOGRAFIJA

Ime i prezime: **Ljiljana Vučković**

Rođena sam 22. novembra 1973. godine u Kotoru, gdje sam završila Osnovnu školu i Gimnaziju (matematičko-programerski smjer). Dobitnik sam Diplome Luča. Tokom osnovnog i srednjeg obrazovanja učestvovala sam na republičkim i saveznim takmičenjima iz prirodnih nauka, na kojima sam imala zapažene rezultate. U Kotoru sam savšila i osnovno muzičko obrazovanje.

Medicinski fakultet Univerziteta u Beogradu sam upisala 1992. godine. Na istom fakultetu sam diplomirala 1999. godine sa prosječnom ocjenom 9,26.

Magistarske studije sam upisala školske 2000/01. godine na Medicinskom fakultetu, Univerziteta u Beogradu. Magistarsku tezu pod nazivom "Imunohistohemijska analiza parafolikularnih-C ćelija u koloidnoj strumi štitaste žlijezde" sam odbranila 3. juna 2004. godine.

Specijalizaciju iz oblasti Patološke anatomije sam upisala na Medicinskom fakultetu, Univerziteta u Novom Sadu školske 2002/03. Specijalistički ispit sam položila 8. novembra 2005. godine sa odličnom ocjenom.

Doktorsku disertaciju pod nazivom "Angiogeneza i ekspresija VEGF, EGFR i MMP9 u skvamoznom karcinomu bronha i njihov značaj u prognozi bolesti" sam odbranila 19. septembra 2008. godine.

Zvanje subspecijaliste iz oblasti Medicinske citologije stekla sam 8. jula 2011. na Medicinskom fakultetu Univerziteta u Novom Sadu.

Zakonom obavezan staž sam odradila od 26. novembra 1999. do 26. novembra 2000. godine u Domu zdravlja Kotor i položila stručni ispit februara 2001. godine.

Od 12. marta 2001. godine sam zaposlena na Medicinskom fakultetu u Podgorici kao stručni saradnik na Katedri za patologiju. Od školske 2004/05. sam angažovana na Medicinskom fakultetu u Podgorici, kao saradnik u nastavi na predmetu Patologija, studijski program Medicina i na predmetima Patologija i Oralna patologija, na studijskom programu Stomatologija.

Školske 2002/03., 2003/04. i 2004/05. sam bila angažovana kao asistent na predmetima Patologija i Oralna patologija na Stomatološkom fakultetu, Univerziteta Istočno Sarajevo u Foči.

Od školske 2009/10. sam angažovana na Fakultetu primijenjene fizioterapije u Igalu, na predmetu Patologija sa patofiziologijom za organizovanje i sprovođenje teorijske nastave, a od šk. 2011/12. godine i na predmetu Histologija na istom fakultetu.

Aprila 2002. godine zasnivam radni odnos u Centru za patologiju Kliničkog centra Crne Gore u Podgorici.

Nakon uspješno odrađenih specijalističkih studija, od novembra 2005. godine radim kao specijalista patološke anatomije u Centru za patologiju Kliničkog centra Crne Gore, a od jula 2011. godine i kao subspecijalista citolog.

U zvanje docent na Univerzitetu Crne Gore izabrana sam 2013. godine. U zvanje vanrednog profesora za oblast Histologija i embriologija, na Univerzitetu Crne Gore sam izabrana 2019. godine.

Načelnik sam Odjeljenja citologije u Centru za patologiju, Kliničkog centra Crne Gore.

Dana 21.12.2017.godine Senat Univerziteta u Novom Sadu imenovao me je za mentora na izradi doktorske disertacije pod nazivom „Proteinska ekspresija i genska amplifikacija receptora humanog epidermalnog rasta 2 (HER2) kod adenokarcinoma pluća" kandidata dr Mirjane Miladinović. Doktorska disertacija je odbranjena na Medicinskom fakultetu, Univerziteta u Novom Sadu 11.1.2019. godine.

Kao stipendista Univerziteta Crne Gore boravila sam 2008. godine u Univerzitetskoj bolnici u Kardifu, Vels, Velika Britanija.

Učestvovala sam na brojnim nacionalnim i međunarodnim seminarima i kongresima.

Član sam nekoliko nacionalnih i međunarodnih projekata.

Član sam Uređivačkog odbora, Univerziteta Crne Gore.

Član sam Radne grupe Ministarsta zdravlja za organizaciju i sprovođenje programa za ranu detekciju karcinoma grlića materice.

Član sam Ljekarske komore Crne Gore i Evropskog udruženja patologa.

BIBLIOGRAFIJA

Prof. dr Ljiljana Vučković

1.Sjekloća N. Tomić S. Mrklić I. Vukmirović F. ***Vučković Lj.*** Lovasić Belas I. Šimunić Maras M. Prognostic value of IMP3 immunohistochemical expression in triple negative breast cancer. Medicine 2020; 99:7.

2. Borozan S. ***Vučković Lj.*** Smolović B. Nonsteroidal anti-inflammatory drug-induced colopathy in a colorectal cancer screening program. Med Princ Pract Med Princ Pract. 2019;28(2):193-5.

3. Restović I, Bočina I, Vukojević K, Kero D, Filipović N, Raonić J, Vučinić J, Vukmirović F, ***Vučković LJ***, Saraga-Babić M. Time course and expression pattern of the neuronal markers in the developing human spinal cord.Int J Dev Neurosci 2019; 74:1-10.

4. ***Vučković Lj.*** Radović S, Sorat N, Filipović A. Cervical thymic cyst: case report. HK J Paediatr (new series) 2019;24:158-60.

5. Vujošević S, Krnjević Đ, Bogojević M. ***Vučković Lj.*** Filipović A, Dunđerović D, Sopta J. Primary leiomyosarcoma of the thyroid gland with prior malignancy and radiotherapy. A case report and review of literature. World J Clin Cases 2019; 7(4):473-81.

6. ***Vučković Lj.*** Crnogorac N, Panjković M, Miladinović M, Vuksanović Božarić A, Filipović A, et al. Comparison of cytological categories atypical (C3) and suspected (C4) with histopathological diagnosis of breast lesions. JBUON 2018; 23(2):366-71.

7. Vuksanović Božarić A, Abramović M, ***Vučković Lj.*** Golubović M, Vukčević B, Radunović M. Clinical significance of understanding lateral and medial circumflex femoral artery origin variability. Anat Sci Int 2018; doi: 10.1007/s12565-018-0434-1.

8. Matić S, Rakočević M, Jocić T, Todorović M, ***Vučković Lj.*** Jančić S, et al. Clinical significance of microvessel density and proliferation in prostate cancer core biopsy. JBUON 2017; 22(3):757-765.

9. Filipović A, ***Vučković Lj.*** Lymphocytic infiltration as a prognostic factor in papillary thyroid carcinoma. Srp Arh Celok Lek 2017; doi: https: //doi.org/ 10.2298/ SARH170509173F.

10. Lazović R, Smolović B, ***Vučković Lj.*** Radunović M. Preoperative misdiagnosed GISTsurgical transferred into gastric duplication cyst. Vojnosanit Pregl 2016; doi:10.2298/VSP151102305L.

11. Filipović A, ***Vučković Lj.*** Pejakov Lj. Paraganglioma of the thyroid gland: A case report. Vojnosanit Pregl 2014; 71(9): 875-878.

12. Smolović B, Stanisavljević D, Globović M, ***Vučković Lj.*** Miličić B, Djuranović S. Bleeding ulcers in patients without Helicobacter Pylori infection and without exposure to non-steroidal anti-inflammatory drug. Vojnosanit Pregl 2014; 71(2):183-90.

13. Filipović A, ***Vučković Lj.*** Mijović M. Invasive follicular thyroid carcinoma infiltrating trachea. Vojnosanit Pregl 2011; 68(10): 891-894.

14. Zvrko E, Mikić A, ***Vučković Lj.*** Đukić V, Knežević M. Prognostic relevance of CD105-assessed micro-vessel density in laryngeal carcinoma. Otolaryngol Head Neck Surg 2009; 141(4): 478-483.

15. Zvrko E, Mikić A, ***Vučković Lj.*** Clinicopathological significanse of CD105-assessed micro-vessel density in glotic laryngeal squamous cell carcinoma. Auris Nasus Larynx 2009; 37: 77-83.

16. Zvrko E, Mikić A, ***Vučković Lj.*** CD105 expression in glotic laryngeal squamous cell carcinoma. Eur Arch Otorhinolaryngol 2009; 266(7):1053.

PROJEKTI:

1. Erasmus+ project: "School-to-Work Transition for Higher education students with disabilities in Serbia, Bosnia & Herzegovina and Montenegro – Trans2Work". Univerzitet Crne Gore, 2015-2018.

2. Ministrastvo nauke Crne Gore, bilateralni projekat: „procjena kvaliteta života pacijenata sa tumorsima nadbubrežne žlijezde, prije i nakon hirurškog liječenja". Partneri: Klinički centar Crne Gore i Medicinski fakultet, Univerzitet u Beogradu. 2017-2018.

3. Ministrastvo nauke Crne Gore, bilateralni projekat „Mitohondrijalna disfunkcija u rastu carcinoma, rezistenciji na ljekove i hemoterapijom indukovanoj neuropatiji". Partneri: Medicinski fakultet Univerziteta Crne Gore i Institut za biomembrane i bioenergiju, Bari, Italija. 2017-2018.

4. Ministarstvo nauke Crne Gore, nacionalni projekat: „ Nove metode za stratifikaciju rizika za progresiju kancera i Alchajmerove bolesti kod pacijenata u Crnoj Gori – DEMONSTRATE". Medicinski fakultet, Univerzitet Crne Gore, 2019-2021.

Број: 04-29/11
Нови Сад, 22. септембар 2022. године

На основу члана 58 став 3 тачка 5 и члана 75 Закона о високом образовању („Службени гласник РС" број 88/2017, 27/2018 – др. закон, 73/2018, 67/2019, 6/2020 – др. закони, 11/2021 - аутентично тумачење, 67/2021 и 67/2021 - др. закон), члана 67 став 1 тачка 5 Статута Универзитета у Новом Саду број 01-141/1 од 28. јануара 2022. године, чланова 2, 3 и 4 Правилника о ближим минималним условима за избор у звање наставника на Универзитету у Новом Саду број 01-134/4 од 25. фебруара 2021. године и члана 7 Правилника о начину и поступку стицања звања и заснивања радног односа наставника Универзитета у Новом Саду број 04-179/7 од 12. јула 2018. године, Сенат Универзитета у Новом Саду на седници одржаној 22. септембра 2022. године, једногласно је донео

О Д Л У К У

Др Драгана Тегелтија бира се у звање ванредног професора за ужу научну област Патологија на Медицинском факултету Нови Сад Универзитета у Новом Саду.

Одлука се примењује од дана закључења уговора о раду лица изабраног у звање наставника из става 1 ове одлуке са деканом Факултета.

О б р а з л о ж е њ е

На основу одлуке декана Медицинског факултета Нови Сад Универзитета у Новом Саду објављен је конкурс за избор наставника у звање ванредног професора за ужу научну област Патологија на Медицинском факултету Нови Сад Универзитета у Новом Саду. Конкурс је објављен у листу Послови дана 23. марта 2022. године.

На објављени конкурс пријавила се кандидаткиња: др Драгана Тегелтија.

Одлуком Наставно-научног већа Медицинског факултета Нови Сад Универзитета у Новом Саду број 05-14/44-2022/5-12 од 12. априла 2022. године именована је Комисија за писање реферата о пријављеним кандидатима за избор у звање наставника, у следећем саставу:

- Др Дејан Вучковић, редовни професор Медицинског факултета Нови Сад Универзитета у Новом Саду (ужа научна област Патологија)
- Др Бојан Зарић, ванредни професор Медицинског факултета Нови Сад Универзитета у Новом Саду (ужа научна област Интерна медицина (Пулмологија))
- Др Сандра Тривунић Дајко, ванредни професор Медицинског факултета Нови Сад Универзитета у Новом Саду (ужа научна област Патологија)
- Др Мирјана Живојинов, ванредни професор Медицинског факултета Нови Сад Универзитета у Новом Саду (ужа научна област Патологија)
- Др Татјана Терзић, ванредни професор Медицинског факултета Универзитета у Београду (ужа научна област Патологија)

Комисија за писање реферата о кандидатима за избор у звање наставника је дана 22. јула 2022. године доставила Изборном већу Медицинског факултета Нови Сад Универзитета у Новом Саду,

реферат број 02-21/1977/А од 22. јула 2022. године у коме је предложила да се др Драгана Тегелтија изабере у звање ванредног професора.

Реферат Комисије стављен је на увид јавности 1. августа 2022. године, објављивањем на интернет страници Универзитета у Новом Саду, у Билтену бр. 1655 од 1. августа 2022. године.

Изборно веће Медицинског факултета Нови Сад Универзитета у Новом Саду на седници одржаној 12. септембра 2022. године утврдило је резултате рада:

1. обавезни елементи:
1.1. Способност за наставни рад или резултати у наставном раду у претходном изборном периоду
1.2. Способност за научно-истраживачки, односно уметнички рад или резултати у научно-истраживачком, односно уметничком раду у претходном изборном периоду
2. изборни елементи:
2.1. Стручно-професионални допринос
2.2. Допринос академској и широј заједници
2.3. Сарадња са другим високошколским, научно-истраживачким, односно институцијама културе или уметности у земљи и иностранству

и утврдило Предлог одлуке о избору др Драгане Тегелтије у звање ванредног професора.

Медицински факултет Нови Сад Универзитета у Новом Саду доставио је документацију прописану чланом 4 Правилника о начину и поступку стицања звања и заснивања радног односа наставника Универзитета у Новом Саду Стручном већу за медицинске науке Сената Универзитета у Новом Саду.

Стручно веће за медицинске науке Сената Универзитета у Новом Саду на седници одржаној електронским путем са роком за изјашњавање до 19. септембра 2022. године дало је позитивно мишљење о предлогу одлуке о избору др Драгане Тегелтије у звање ванредног професора.

Имајући у виду сву достављену документацију, Сенат Универзитета је на седници одржаној 22. септембра 2022. године једногласно донео одлуку да се др Драгана Тегелтија изабере у звање ванредног професора за ужу научну област Патологија на Медицинском факултету Нови Сад Универзитета у Новом Саду.

ПОУКА О ПРАВНОМ ЛЕКУ:

Ова одлука је коначна и против ње незадовољни учесници Конкурса могу покренути управни спор пред Управним судом у Београду, Немањина 9, у року од 30 дана од дана пријема. За подношење тужбе за покретање управног спора предвиђена је такса у износу од 390 динара.

Проф. др Дејан Мадић
Председник Сената Универзитета

Одлуку доставити:
1. Лицу изабраном у звање наставника путем Факултета
2. Медицинском факултету Нови Сад Универзитета у Новом Саду
3. Архиви Универзитета у Новом Саду

LIČNE INFORMACIJE

Dragana Tegeltija

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E-mail: tegeltijadragana@gmail.com

Državljanstvo: Srbije

Datum rođenja: 20.08.1969. Ključ, Bosna i Hercegovina

RADNO ISKUSTVO

Od 2011-trenutno,

- Institut za plućne bolesti, Put doktora Goldmana 4, Sremska Kamenica,
- Služba za patološko-anatomsku i molekularnu dijagnostiku,
- Patolog,
- Citolog.

od 2012 - trenutno,

- Medicinski fakultet Univerziteta u Novom Sadu, Hajduk Veljkova 3, Novi Sad,
- Katedra za patologiju,
- Vanredni profesor 2022.- trenutno,
- Docent od 2017.- 2022.,
- Asistent od 2012-2017.

od 2012-2013.

- Medicinski fakultet Foča Univerziteta u Istočnom Sarajevu, Studentska 5, Foča,
- Katedra za patologiju,
- Asistent.

Od 2021- trenutno

- Medicinski fakultet Foča Univerziteta u Istočnom Sarajevu, Studentska 5, Foča,
- Katedra za patologiju,
- Docent,
- Vanredni profesor.

Od 2011- trenutno

- Zavod za laboratorijsku dijagnostiku Biotest, Koste Abraševića 31, Novi Sad.

2001-2011.

- Opšta bolnica Vrbas, dr Milana Čekića, Vrbas,
- Služba za patologiju,
- Patolog,
- Citolog,
- Načelnik službe za patologiju i citologiju (2004-2011.),
- Upravnik sektora zajedničkih medicinskih delatnosti (2006-2008.),
- Pomoćnik direktora za medicinska pitanja (2008-2011.).

2005-2014.

- Srednja medicinska škola Kozma i Damjan, Njegoševa, Vrbas,
- Nastavnik predmeta: patologija, interna medicina i hirurgija.

1997-2001.

- Dom zdravlja Srpska Crnja, Patrijarha Arsenija Čarnojevića 15, Srpska Crnja,
- Doktor medicine.

1995-1997.

- Dom zdravlja Prijedor, ulica Vožda Karađorđa 2, Prijedor.

1995-1995.

- Dom zdravlja Ključ, Šehićka 1, Ključ,
- Doktor medicine.

OBRAZOVANJE I OSPOSOBLJAVANJE

2010-2013.

- Medicnski fakultet Univerzitet u Novom Sadu, Doktorske studije,

2016.

- Odbranjena doktorska disertacija: „ Učestalost i tipovi mutacija epidermalnog faktora rasta u invazivnim adenokarcinomima pluća,
- Doktor nauka,
- Odličan uspeh.

2008-2009.

- Medicnski fakultet Univerzitet u Novom Sadu, Subspecijalističke studije,
- Medicinska citologija.

2010.

- Odbranjen subspecijalistički rad iz medicinske citologije: „Pleuralni izlivi-dijagnostički principi i dileme"
- Subspecijalista medicinske citologije,
- Odličan uspeh.

2001-2004.

- Medicnski fakultet Univerzitet u Novom Sadu, Specijalističke studije,
- Patološka anatomija,
- Specijalista patološke anatomije,
- Odličan uspeh.

1989-1995.

- Medicnski fakultet Univerzitet u Sarajevu (1988/89-1992.) i Medicnski fakultet Univerzitet u Banja Luci (1992-1995.),
- Doktor medicine,
- Prosečna ocena - 8.33

1985-1988

- Srednjoškolski centar Lazar Đukić, Ključ Hemijski tehničar analitičar,
- Odličan uspeh,

1981-1988

- Osnovna škola Nikola Mačkić, Ključ,
- Odličan uspeh (đak generacije).

OBUKE/KURSEVI/SEMINARI

- *Aktivno i pasivno učešće na brojnim stručnim i naučnim skupovima sa međunarodnim učešćem,*

  Organizovala sam predavanja o malignim bolestima žena u saradnji sa Udruženjem dobrovoljnih davalaca krvi iz Malog Iđoša (2007.),
- *Organizovala sam predavanje o karcinomu dojke u Vrbasu pod pokroviteljstvom Opšte bolnice Vrbas (2010.)*

- *Predavač u školi cervikalne citologije u organizaciji medicinskog fakulteta u Novom Sadu (2013-2019.),*
- *Polaznik kursa PD-L1 testiranju (2018., 2023.).*
- *Polaznik kursa za trenera PD-L1 testiranja (2023.)*

RAD NA RAČUNARU

- Poznajem rad na računaru i koristim MS Office paket (Word, Exel i Power Point - napredni nivo znanja)

JEZICI

- Maternji jezik - srpski
- Završen B1 kurs engleskog jezika, škola engleskog jezika, Novi Sad,
- Ruski jezik čitam, pišem i govorim na osnovnom nivou.

LIČNE OSOBINE/HOBIJI

- 1995-1988. - stoni tenis i košarka,
- 2001-2011. - košarka i odbojka,
- od 2011- trenutno – individualna rekreacija,
- volim životinje - kućni ljubimac mačk Đus (10 godina),
- volim prirodu,
- volim ručne radove,
- volim da kuvam.

OSTALE NAPOMENE

- Analitična,
- Komunikativna,
- Elokventna,
- Precizna,
- Odgovorna,
- Poseduje takmičarski duh,
- Spremna za timski rad,
- Uporna,
- Član etičkog odbora Regionalne lekarske komore Vojvodine u prvom sazivu,

- Član Srpskog lekarskog društva društva lekara Vojvodine (2001-trenutno),
- Dobitnik Zahvalnice SLD DLV,
- Dobitnik Diplome SLD DLV,
- Dobitnik Povelje SLD DLV,
- Član etičke komisije za ocenu etičnosti teme doktorskih disertacija Medicinskog fakulteta Univerziteta u Novom Sadu (2018-trenutno),
- Član komisije za prijemi ispit Medicinskog fakulteta Univerziteta u Novom Sadu (2015-trenutno),
- Od 2001 – trenutno preko 100 objavljenih stručnih i naučnih radova,
- od 108 naučno-stručnih radova sledećih 17 se nalazi na SCI listi:
- Mentor na specijalističkim studijama (tri kandidata,)
- Mentor na subspecijalističkim studijama (četiri kandidata),
- Mentor i komentor na doktorskim studijama (četiri kandidata),
- Mentor na završnom diplomskom radu (devet kandidata),
- Član komisije za odbranu diplomskog rada (15 kandidata),
- Mentor u studentskim radovima (trinaest kandidata),
- Član komisije za recenziju studentskih radova na studentskim kongresima sa međunarodnim učešćem (od 2017-trenutno),
- Učesnik gradskog projekta „Tvoje zdravlje u tvojim rukama“ (od 2018-trenutno),
- Živim u dvosobnom stanu sa Dragoslavom Dvizcem 25 godina,
- Majka muškog deteta Stefana starog 27 godine koji živi odvojeno u Novom Sadu,
- Učesnik Omladinske radne akcije Beograd (1986.),
- Nosilac Titove štafete (1986.)
- Od 1985-1988. predsednik Opštinske omladinske organizacije.

VOZAČKA DOZVOLA

- Poseduje vozačku dozvolu B kategorije.

Radovi.

1. Zaric B, Stojsic V, Panjkovic M, **Tegeltija D**, Stepanov V, Kovacevic T, et al. Clinicopathological features and relation between anaplastic lymphoma kinase (ALK) mutation and histological subtype of lung adenocarcinoma in Eastern European Caucasian population. J Cancer. 2016;7(15):2207-12. (M22).

2. **Tegeltija D,** Lovrenski A, Stojanović G, Bijelović M, Jeličić I, Eri Ž. Inflammatory myofibroblastic tumours of the respiratory tract: a series of three cases with varying clinical presentations and treatment. Srp Arh Celok Lek. 2015;143(7-8):458-63. (M23).

3. Lovrenski A, Eri Ž, **Tegeltija D**, Kašiković-Lečić S, Panjković M. Desquamative interstitial pneumonia-a case report and review of the literature. Srp Arh Celok Lek. 2014;142(9-10):602-6. (M23).

4. Lovrenski A, Đurić M, Klem I, Eri Ž, Panjković M, **Tegeltija D**, et al. Multisystem Langerhans cell histiocytosis coexisting with metastasizing adenocarcinoma of the lung-case report. Vojnosanit Pregl. 2013;70(12):1159-61. (M23).

5. Panjković M, Lovrenski A, Eri Ž, Knežević-Ušaj S, **Tegeltija D**, Krčedinac J. The role of immunohistochemical evaluation in the diagnosis of malignant mesothelioma of the pleura. Vojnosanit Pregl. 2013;70(11):1010-4. (M23)

6. Andrejević-Višnjić B, **Tegeltija D,** Lovrenski A, Vučković D, Samardžija G, Tadić Latinović LJ. Mediastinal metastasis of primary extraneural ependyomoma: case report. Vojnosanit Pregl. 2018 DOI: https://doi.org/10.2298/VSP181023181A6. (M23)

7. **Tegeltija D**, Lovrenski A, Vasiljević T, Samardžija G, Kuhajda I. Exogenous lipoid pneumonia mimicking multifocal subpleural tumors. Srp Arh Celok Lek. 2019. https://doi.org/10.2298/SARH180410070T (M23)

8. Lovrenski A, Ilić A, Kuhajda I, **Tegeltija D**, Lovrenski J. Intrapulmonary solitary fibrous tumor. Srp Arh Celok Lek. 2019. https://doi.org/10.2298/SARH181117056L.(M23)

9. Lovrenski A, Vasilijević M, Panjković M,**Tegeltija D,** Vučković D, Baroš I, Lovrenski J. Sclerosing Pneumocytoma: A Ten-Year Experience at a Western Balkan University Hospital. Medicina 2019, 55, 27. (M22)

10. **Tegeltija D**, Lovrenski A, Vasiljević A, Andrejić-Višnjić B. Adequacy of biopsy samples for EGFR molecular testing in lung adenocarcinoma. Vojnosanit Pregl. 2019. DOI: https://doi.org/10.2298/VSP181225083T (M23)

11. Lalić N, Tegeltija D, Kuhajda I, Tomić S, Lalić I. Metastatic atypical lung carcinoid treated with combined therapies. Srp Arh Celok Lek. 2019 Nov-Dec;147(11-12):769-772 (M23)

12. Džambas J, Aleksić I, Škuletić V, Cerović S, Tegeltija D. Correlation between cytological and histopathological diagnosis of non-small cell lung cancer and accuracy of cytology in diagnosis of lung cancer. Vojnosanit Pregl. In press. DOI: 10.2298/VSP200618117D. (M23)

13. **Tegeltija D**, Lovrenski A, Vasiljević T, Maksimović S. Association between epidermal growth factor receptor mutation status, clinicopathological characteristics and TTF-1 expression in lung adenocarcinoma: A single center study. Srp Arh Celok Lek. 2021;149(3-4):174-8. (M23)

14. **Tegeltija D**, Samardzija G, Vasiljevic T, Zaric B, Djuric D, Eri Z. A case report of complete consolidation of the right middle lobe due to the endobronchial fibroma. In: 27th European Congress of Pathology; 2015 Sep 5-9; Beograd, Serbia. Virchows Arch. 2015;467:257. (M34)

15. Samardzija G, Cemerlic-Adjic N, Panic G, Tadic S, Nikin Z, Lovrenski A, **Tegeltija D**, Miladinovic M, Jelicic I. Amyloidosis of epicardial and intramural coronary arteries as an unusual cause of myocardial infarction: a case report. In: 27th European Congress of Pathology; 2015 Sep 5-9; Beograd, Serbia. Virchows Arch. 2015;467:109. (M34)

16. Vuckovic-Hardi L, **Tegeltija D**, Milic M, Bulatovic V, Lakic T, Jelicic I. Malignant Brenner tumour. In: 27th European Congress of Pathology; 2015 Sep 5-9; Beograd, Serbia. Virchows Arch. 2015;467:146-7. (M34)

17. Druzsek G, Eri Z, **Tegeltija D**, Skrbic D. "Undifferentiated" small round cell tumours of the sinonasal tract. Differential diagnosis update: a case report. In: 27th European Congress of Pathology; 2015 Sep 5-9; Beograd, Serbia. Virchows Arch. 2015;467:75. (M34)

18. Milic M, Jelicic I, Bozanic S, **Tegeltija D**, Solajic N, Samardzija G. A case report of very rare synchronous multicentric papillary and medullary carcinoma of thyroid gland. In: 27th European Congress of Pathology; 2015 Sep 5-9; Beograd, Serbia. Virchows Arch. 2015;467:72. (M34)

19. Lovrenski A, Panjković M, Eri Ž, **Tegeltija D**, Samardžija G. Solitary fibrous tumor of the pleura: series of cases. In: 25th European Congress of Pathology; 2013 Aug 30-Sep 4; Lisbon; Portugal. Virchows Arch. 2013;463(2):241. (M34)

20. Lovrenski A, **Tegeltija D,** Panjkovic M, Eri Ž, Jeličić I. Thymoma: evaluation of clinical and pathological characteristics of 27 cases. In: 25th European Congress of Pathology; 2013 Aug 30-Sep 4; Lisbon; Portugal. Virchows Arch. 2013;463(2):192. (M34)

21. Jeličić I, **Tegeltija D**, Lovrenski A, Panjković M, Eri Živka. Correlation of bronchial brushing cytology with bronchial biopsy in diagnosis of lung cancer. In: 25th European Congress of Pathology; 2013 Aug 30-Sep 4; Lisbon; Portugal. Virchows Arch. 2013;463(2):270. (M34)

22. Jeličić I, **Tegeltija D**, Lovrenski A, Panjković M, Eri Ž, Jeličić B. Our experience with CT-guided transthoracic fine needleaspiration cytology of peripheralpulmonary lesions. In: 25th European Congress of Pathology; 2013 Aug 30-Sep 4; Lisbon; Portugal. Virchows Arch. 2014;465(1):379. (M34)

23. Ratković V, **Tegeltija D**, Lovrenski A. Rhabdomyosarcoma of the oral cavity: a case report. In: 8th International Medical Students' Congress (IMSCNS); 2013 Jul 18-21; Novi Sad; Serbia; 2013. p. 119. (M34)

24. Vasiljevic T Eri Zivka Tegeltija Dragana R Samardzija Golub. Causes of death in patients with lung cancer. In: **29**th European Congress of Pathology; 2017 **Aug 30-Sep 4**; Amsterdam; (M34)

25. Sekerus Vanesa Stojanovic Goran Bursac Daliborka S Tegeltija Dragana R Stolic M Andrijevic Ilija. Cell-free circulating tumor DNA in plasma of non-small cell lung cancer patients: The role in EGFR T790 M mutation testing (M34).

26. **Tegeltija D**, Lovrenski A, Panjković M, Eri Ž, Klem I. Testicular (gonadal stromal) fibroma: case report. Arch Oncol. 2012;20(1-2):26-7. (M51)

27. **Tegeltija D**, Lovrenski A, Panjković M, Marjanov J, Samardžija G, Pejaković N. Carcinoma developing in a branchial cyst. Med Pregl. 2013;66(3-4):177-80. (M51)

28. Lovrenski A, Panjković M, **Tegeltija D**, Tadić-Latinović Lj, Krčedinac J. Uloga citološke analize pleuralnog izliva u dijagnostici malignog mezotelioma. Med Pregl. 2012;65(1-2):5-8. (M51)

29. **Tegeltija D**, Lovrenski A, Panjković M, Knežević-Ušaj S, Eri Ž, Klem I. Clear cell sarcoma of the nuchal region with metastasis in stomach. Arch Oncol. 2011;19(3-4):76-8. (M52)

30. Anđelković A, **Tegeltija D**, Anđelković D, Ergelašev I. Askinov tumor. Respiratio. 2014;4(1-2):202-6. (M52)

31. Maksimović O, Vrtunski More L, Papović J, Stojanović G, **Tegeltija D**. Karcinoid bronha-prikaz slučaja. Respiratio. 2015;5(1-2):248-52. (M52)

32. Lovrenski A, Jeličić I, **Tegeltija D**, Koledin M, Bijelović M, Panjković M. Solitarni fibrozni tumor pleure – prikaz serije slučajeva i pregled literature. Respiratio. 2017; 7(1-2): 1-8.

33. **Tegeltija D,** Krajnović B, Krup J, Maksimović S, Gardić N, Dejan M, Lovrenski A, Ćuk M. Prezentacija 24 slučaja karcinoida pluća - studija jednog centra; Respiratio 2023, 13, (1-2) 315-22.

34. Lovrenski A, **Tegeltija D,** Jeličić I, Bijelović M, Đurić D, Panjković M. Evaluation of clinical, morphological and pathohisthological characteristics of tymomas – our ten year experience. Arch Oncol. 2017;23(2):20-4. (M52)

35. **Tegeltija D,** Vasiljević T, Samardžija G, Lovrenski A, Kuhajda I, Radovanović B, Vujasinović G, Nikin Z, Eri Ž. Pulmonary alveolar proteinosis – case report. Respiratio. 2018; 8(1-2): 169-74. (M52)

36. Tepavac A, Stanić J, Koledin M, Koledin B, **Tegeltija D,** Vujasinović G. Metastatic synovial sarcma in the lungs – case report. Respiratio. 2018; 8 (1-2): 203.07.(M52)

37. **Tegeltija D**, Lovrenski A, Milić M, Koledin M, Panjkovć M. Sclerosing hemangioma of the lung. Arch Oncol. 2013;21(3-4):144-6. (M52)

38. **Tegeltija D,** Samardžija G, Lovrenski A, Eri Ž, Popović M. Tačnost citološke analize u dijagnostici malignih oboljenja pleure. MD- Mediacal Data. 2017;9(4):229-33 (M52)

39. **Tegeltija D**, Bijelović M, Samardžija G, Vasiljević T. Symptomatic pleural lipoma. Arch Oncol. 2018; 24 (2): 24-5. (M52)

40. Pupavac U, **Tegeltija D**, Lovrenski A, Sekeruš V, Maksimović S, Bijelović M, Oluški D. Kliničko-patološke karakteristike malignog pleuralnog mezotelioma – naše petogodišnje iskustvo. MD-Medical Data 2019;11(1): 019-22. (M51)

41. Lovrenski A, **Tegeltija D**, Vrekić Ž, Andrejić Višnjić B, Maksimović S, Považan A. Patohistološka i serološka dijagnoza u plućnim oblicima bolesti izazvanih gljivicama iz roda aspergillus. MD-Medical Data 2018;10(4): 191-6. (M51)

42. Lovrenski A, Kašiković Lečić S, Dragišić D, Novković Ostojić S, **Tegeltija D**. Istovremena pojava sarkoidoze i adenocarcinoma pluća-prikaz slučaja. Respiratio. 2019; 9 (1-2):191-94.(M52)

43. Lovrenski A, **Tegeltija D,** Pena Karan S, Maksimović S, Kašiković Leečić S, Kuhajda I. Biopsija pluća u dijagnozi intersticijalnih plućnih oboljenja. Respiratio. 2019; 9 (1-2):23-29.(M52)

44. Maksimović S, Bijelović M, **Tegeltija D,** Lovrenski A, Ergelašev I, Simetić V. Švanom interkostalnih nerava. Respiratio. 2019; 9 (1-2):241-46. (M52).

45. **Tegeltija D,** Lovrenski A, Vasiljević T, Sekeruš V, Maksimović S, Kuhajda I, Bijelović M, Ivanić M, Ilić M. Da li je histološka građa adenocarcinoma pluća u dijagnostičkim i terapijskim uzorcima identična? Respiratio. 2019; 9 (1-2):30-5.(M52).

46. Samardžija G, Popović M, Lovrenski A, Miljković D, **Tegeltija D**. Papilary fibroelastoma of the heart – 10 years experience from Institute of Cardiovascular Diseases, Sremska Kamenica. MD-Medical Data 2019;11(2): 087-091.(M51)

47. Vrekić Ž, Lovrenski A, **Tegeltija D**, Novković Ostojić S, Krajnović B, Považan A. MD-Medical Data 2019;11(2): 093-097. (M51).

48. Novković Ostojić S, Vujasinović G, Sazdanić Velikić D, **Tegeltija D**, Prvulović Bunović N, Mihailović J, Sečen N. GIGANTSKA BULA I KARCINOM PLUĆA. MD-Medical Data 2020;12(3): 161-164 (M51).

49. **Tegeltija D**, Krajnović B, Sekeruš V, Stojanović G, Zarić B, Lovrenski A, Miljković D,Vasiljevićć T, Maksimović S. NAŠA PRVA ISKUSTVA U EVALUACIJI PD-L1 EKSPRESIJE. MD-Medical Data 2021;13(2): 059-064 (M51).

50. Panjković M, Eri Ž, **Tegeltija D**. Uloga izrade ćelijskih blokova u dijagnostici plućnih oboljenja. Pneumon. 2013;50:39-43. (M53)
51. Bokan A, Tegeltija D, Kopitović I, Golić A, Vukoja M. Faktorimrizika za razvoj plućne tromboembolije . desetogodišnja autopsijska studija. Medicina danas. 2018; 17 (4-6):50-58 (M53)

52. **Tegeltija D**, Lovrenski A. Cytological analisys of pleural effusions. In: 2nd Congress of Pathologist in BiH with International Participation; 2012 May 10-12; Banja Luka, Republic of Srpska; 2012. p. 166-7. (M64)

53. Đurić G, **Tegeltija D**, Panjković M, Lovrenski A, Milić M. Synchronous presence of hamartoma and squamous cell carcinoma of the lung. In: 2nd Congress of Pathologist in BiH with International Participation; 2012 May 10-12; Banja Luka, Republic of Srpska; 2012. p. 255-6. (M64)

54. Lovrenski A, Panjković M, **Tegeltija D**, Milić M, Đurić G. Coexistance of inflammatory pseudotumor of the lung and sarcoidosis. In: 2nd Congress of Pathologist in BiH with International Participation; 2012 May 10-12; Banja Luka, Republic of Srpska; 2012. p. 257-8. (M64)

55. **Tegeltija D**, Lovrenski A, Panjković M, Milić M, Stanković M. Pleomorphic hyalinizing angiectatic tumor (PHAT). In: 2nd Congress of Pathologist in BiH with International Participation; 2012 May 10-12; Banja Luka, Republic of Srpska; 2012. p. 269-70. (M64)

56. Milić M, Samardžija G, Lovrenski A, Tegeltija D, Đurić G. Sirenomelia (Mermaid syndrome). In: 2nd Congress of Pathologist in BiH with International Participation; 2012 May 10-12; Banja Luka, Republic of Srpska; 2012. p. 116-7. (M64)

57. **Tegeltija D.** Colorectal carcinoma. In: 1. Kongres patologa Bosne i Hercegovine sa međunarodnim učešćem; 2008 May 13-15; Tuzla, Bosnia and Herzegovina; 2008. p. 69. (M64)

58. Petrović T, **Tegeltija D**, Kovač A, Klem I. Melanoma-case report. In: 1. Kongres patologa Bosne i Hercegovine sa međunarodnim učešćem. 2008 May 13-15; Tuzla, Bosnia and Herzegovina; 2008. p. 73 (M64)

59. Petrović T, **Tegeltija D**. Melanoma our expiriensis. In: 1. Kongres patologa Bosne i Hercegovine sa međunarodnim učešćem; 2008 May 13-15; Tuzla, Bosnia and Herzegovina; 2008. p. 73. (M64)

60. Samardžija G, Kovačević P, Debeljački D, Bjelobrk M, **Tegeltija D**, Nikin Z, Miladinović M. Castleman disease, hyaline vascular type: a case report. In: 1st International Congress of Serbian Pathologists and Cytologists Association; 2016 Apr 21-23; Zlatibor, Serbia; 2016. p. 1570-1. (M64)

61. **Tegeltija D**, Jeličić I, Vasiljević T, Samardžija G, Anđelković D, Eri Ž. Rounded atelectasis. In: 1st International Congress of Serbian Pathologists and Cytologists Association; 2016 Apr 21-23; Zlatibor, Serbia; 2016. p. 1578-9. (M64)

62. Papovic J, Vrtunski-More L, Maksimovic O, Eri Z, **Tegeltija D**, Dragisic D. The most common pulmonary manifestation of rheumatoid arthritis-case report of three patients. In: 4. Kongres respiratorne medicine Srbije sa međunarodnim učešćem; 2015 Oct 15-18; Novi Sad, Srbija. Respiron. 2015;52(Suppl 1):S2576-7. (M64)

63. **Tegeltija D**, Vasiljevic T, Eri Z, Samardzija G, Stepanovic V, Jelicic I. IASLC/ATS/ERS classification of lung adenocarcinoma-analysis of 314 invasive cases. In: 4. Kongres respiratorne medicine Srbije sa međunarodnim učešćem; 2015 Oct 15-18; Novi Sad, Srbija. Respiron. 2015;52(Suppl 1):176-7. (M64)

64. Bokan A, **Tegeltija D**, Lovrenski A. Plućna tromboembolija i komorbiditeti-desetogodišnja autopsijska studija. In: 56. Kongres studenata biomedicinskih nauka Srbije sa internacionalnim učešćem; 2015 Apr 24-28; Vrnjačka Banja, Srbija; 2015. p. 348-9. (M64)

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