DOI: https://doi.org/10.2298/SARH241127007S
UDC: 616.831-006-007.61

ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

Correlation of microRNAs-10b/21/34a expression levels with *IDH1*-mutation status in patients with glioblastoma

Aleksandar Stepanović[1,2], Nina Petrović[3,4], Tatjana Arsenijević[1,2], Marina Nikitović[1,2]

[1]University of Belgrade, Faculty of Medicine, Belgrade, Serbia;
[2]Institute for Oncology and Radiology of Serbia, Department of Radiation Oncology, Belgrade, Serbia;
[3]Institute for Oncology and Radiology of Serbia, Department of Experimental Oncology, Belgrade, Serbia;
[4]University of Belgrade, Vinča Institute of Nuclear Sciences – National Institute of the Republic of Serbia, Belgrade, Serbia;

SUMMARY

Introduction/Objective Isocitrate dehydrogenase (IDH) mutations play a significant role in gliomagenesis. Specific microRNAs, such as microRNA-10b and microRNA-21, act as oncogenic microRNAs, whereas microRNA-34a acts as a tumor suppressor in glioblastoma. Our study aimed to investigate whether the IDH1 mutation status correlates with microRNA-10b, -21, and -34a expression levels in patients with glioblastoma.

Methods The study included 43 patients diagnosed with glioblastoma. We examined microRNA-10b, -21, and -34a expression levels in peripheral blood mononuclear cells after surgery and prior to concurrent radiotherapy with temozolomide, as well as at the 15th and 30th fractions of radiotherapy with temozolomide. Data on IDH1 mutation status were gathered from medical histories and histopathology.

Results Two groups were created to assess the association of microRNA-10b, -21, and -34a expression levels: glioblastoma IDH1-wildtype and glioblastoma IDH1-mutant + not otherwise specified (NOS). The median microRNA-10b expression level before the initiation of concurrent radiotherapy with temozolomide was 130.44 (52.2–622.53) in the IDH1-wildtype group and 94.61 (2.13–816.89) in the IDH1-mutant + NOS group. The median microRNA-21 expression level was 57.16 (2.68–278.98) in the IDH1-wildtype group and 69.74 (4.6–825.43) in the IDH1-mutant + NOS group. The median microRNA-34a expression level was 13.52 (3.16–105.20) in the IDH1-wildtype group and 10.11 (1–210.55) in the IDH1-mutant + NOS group. The results showed no statistically significant difference in the expression levels of microRNA-10b, -21, or -34a between the two groups ($p > 0.05$).

Conclusion Our findings suggest that IDH1 mutation status may not be a critical factor for altered expression of microRNA-10b, -21, and -34a in glioblastoma patients.

Keywords: glioblastoma; microRNA; IDH mutation

INTRODUCTION

Over the past few years, a significant body of research has focused on the molecular and genetic profile of glioblastoma. This combined approach – defined by histopathology, molecular features, and genetic alterations in glioblastoma – led to changes in the World Health Organization (WHO) classification in 2016 and 2021 and a better understanding of tumor biology and clinical behavior of the disease [1, 2].

One of the most important features in the 2016 WHO classification of brain tumors was the inclusion of isocitrate dehydrogenase (IDH) mutation status in glioma classification. Since IDH1 is one of the most important enzymes for cell metabolism, alterations in IDH1 expression or gene mutations can impact enzyme activity and impair cellular metabolism [3]. IDH mutation is considered one of the initial occurrences in the development of astrocytomas and oligodendrogliomas [4]. In fact, research on the sequence of mutations in gliomas shows that IDH mutations occur even before *TP53* mutations in low-grade diffuse astrocytoma and secondary glioblastoma, but they are rare in primary glioblastoma [4]. According to the 2016 WHO classification, glioblastoma was divided into glioblastoma IDH-mutant, WHO grade IV, glioblastoma, IDH-wildtype WHO grade IV, and glioblastoma, Not Otherwise Specified (NOS) WHO grade IV [1]. In 2021, in addition to other parameters for the classification of glioblastoma, any astrocytoma with wildtype IDH is considered glioblastoma, IDH-wildtype, Central Nervous System (CNS) WHO grade IV [2].

MicroRNAs (miRNAs) are non-coding RNAs that play a critical role in gene expression regulation. They bind to incompletely complementary sequences on target messenger RNAs (mRNAs), leading to mRNA degradation or translation inhibition [5]. This mechanism of post-transcriptional regulation enables miRNAs to control various biological processes, such as development, differentiation, proliferation, and apoptosis, and they are among the key regulators of cell metabolism [6]. The expression of microRNAs can be altered by various mutations or regulated through promoter

Received • Примљено: November 27, 2024
Revised • Ревизија: December 30, 2024
Accepted • Прихваћено: January 12, 2025
Online first: January 14, 2025

Correspondence to:
Marina NIKITOVIĆ
Pasterova 14
11000 Belgrade, Serbia
marina.nikitovic@ncrc.ac.rs

methylation [5]. MiRNAs can directly or indirectly target different genes, including IDH. Conversely, IDH mutations after the production of 2-hydroxyglutarate (2-HG) can influence or alter the expression of various miRNAs and regulate tumor development in gliomas [7].

In glioblastoma, specific miRNAs may have significant impact on tumorigenesis, invasiveness, and resistance to therapy. MiR-10b, miR-21, and miR-93 act as oncogenic miRNAs (oncomiRs), while miR-7, -34a, and -128 act as tumor suppressors in glioblastoma, and they target multiple genes [8]. Research has shown that miRNAs can be found in extracellular fluids. They are stable compared to cellular RNA, which is the reason why they can serve as potential biomarkers for various diseases, including cancer [9].

Since mutations in IDH play a role in gliomagenesis, and miRNAs-10b/21 act as oncomiRs and miR-34a acts as a tumor suppressor in glioblastoma, we aimed to investigate whether the IDH mutation status correlates with miRNA-10b/21/34a expression levels in patients with high-grade gliomas (HGGs – glioblastoma). A better understanding of this poorly understood feedback and regulatory mechanism between IDH mutation and miRNAs can yield additional valuable insights into the differing biological behaviors of IDH-mutant versus IDH-wildtype gliomas and possibly have therapeutic implications.

METHODS

This study examined miR-10b, -21, and -34a levels in peripheral blood mononuclear cells (PBMCs) from 43 glioblastoma patients. The 2016 WHO Classification of Tumors of the Central Nervous System was used. Blood samples were taken post-surgery and prior to treatment with concurrent radiotherapy (RT) and chemotherapy with temozolomide (TMZ), and at the 15th and 30th fractions of RT with concurrent TMZ. The study was conducted at the Clinic of Neurosurgery, University Clinical Center of Serbia, and the Institute for Oncology and Radiology of Serbia since October 2017, adhering to the ethical guidelines of the Declaration of Helsinki. The study protocol received approval from the Ethical Research Committee of the Faculty of Medicine, University of Belgrade (approval number 1322/X-39).

After surgery, patients received RT combined with TMZ, followed by adjuvant TMZ. RT began 4–6 weeks post-surgery, with 30 fractions of 2 Gy each, totaling 60 Gy, using either 3D conformal or VMAT technique (Figure 1). Concomitant therapy included 75 mg/m^2 TMZ daily during RT.

The data on IDH1 mutation status were gathered from medical history, histopathology, and immunohistochemistry results.

PBMCs were isolated from heparinized blood using Histopaque-1077 (Sigma-Aldrich, Burlington, MA, USA), and total RNA containing miRNAs was extracted using TRI Reagent(Sigma-Aldrich). RNA quality was assessed using a BioSpec-nano (Shimadzu Corporation, Kyoto, Japan) spectrophotometer, ensuring an A260/280 ratio of 1.7–2.1. Specific TaqMan® (Thermo Fisher Scientific Inc., Waltham, MA, USA) assays were employed to analyze miR-10b, -21, and -34a expression. The comparative delta-delta Ct method was used to calculate relative quantity values, normalizing to RNU6B and calibrating against the sample with the lowest RQ value.

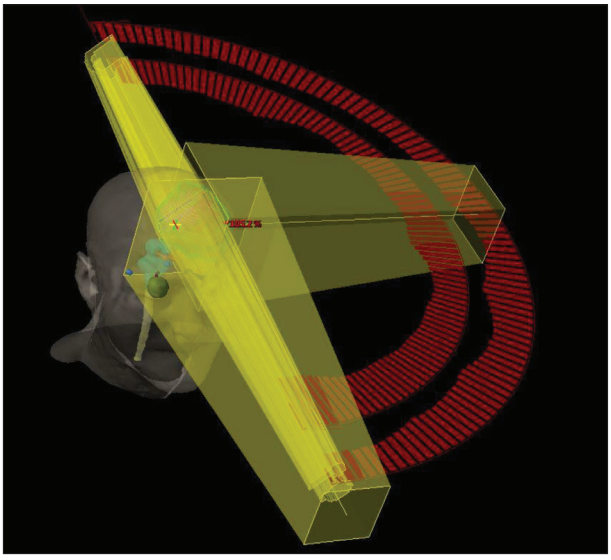

Figure 1. Volumetric modulated arc therapy (VMAT) technique of radiotherapy in a patient with glioblastoma (Institute for Oncology and Radiology of Serbia)

Statistical analysis

The Mann–Whitney U test was used to compare differences between two independent groups. For the analysis of the correlation of the level of expression of miRNA and IDH mutation status, Pearson's and Spearman's tests were used. Log-rank (Mantel–Cox test) was used to examine the significance of the differences. All statistical analyses were conducted using IBM SPSS Statistics, Version 22.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Due to the unfavorable ratio of the number of outcomes to potential predictors, it was not possible to make comparisons among the three groups based on IDH1 status (22 patients had glioblastoma IDH1-wildtype, two patients had glioblastoma IDH1-mutant, and 19 patients had glioblastoma NOS).

According to data from the literature on the prognostic significance of the mutation's presence or absence, two groups were created to assess the association of miR-10b/21/34a expression levels: glioblastoma IDH1-wildtype and glioblastoma IDH1-mutant + NOS.

The median miRNA-10b expression level post-surgery and before the initiation of concomitant RT with TMZ was 130.44 (52.2–622.53) in the IDH1-wildtype glioblastoma group and 94.61 (2.13–816.89) in the IDH1-mutant + glioblastoma NOS group.

The median miRNA-21 expression level was 57.16 (2.68–278.98) in the IDH1-wildtype glioblastoma group and 69.74 (4.6–825.43) in the IDH1-mutant + glioblastoma NOS group.

The median miRNA-34a expression level was 13.52 (3.16–105.2) in the IDH1-wildtype glioblastoma group and 10.11 (1–210.55) in the IDH1-mutant + glioblastoma NOS group.

A complete overview of miRNA-10b/21/34a expression levels in relation to IDH1 mutation status is provided in Table 1.

Table 1. Correlation between miR-10b/21/34a expression levels and IDH1 mutation status

miR	*IDH1*-wild type GB	*IDH1-mutant* + NOS GB	p-value
miR-10b prior RT median (min-max)	130.44 (52.2–622.53)	94.61 (2.13–816.89)	0.234
miR-10b 15f + TMZ median (min-max)	83.35 (16.03–433.53)	100.7 (1–922.88)	0.451
miR-10b 30f + TMZ median (min-max)	131.75 (1.47–493.53)	102.96 (2.32–2751.5)	0.560
miR-21 prior RT median (min-max)	57.16 (2.68–278.98)	69.74 (4.6–825.43)	0.903
miR-21 15f + TMZ median (min-max)	30.53 (2.79–542.32)	70.57 (4.37–960.07)	0.451
miR-21 30f + TMZ median (min-max)	60.56 (1–410.72)	62.03 (3.11–1940.21)	0.981
miR-34a prior RT median (min-max)	13.52 (3.16–105.2)	10.11 (1–210.55)	0.662
miR-34a 15f + TMZ median (min-max)	34.48 (3.48–198.64)	41.93 (4.04–352.38)	0.504
miR-34a 30f +TMZ median (min-max)	51.42 (2.94–363.04)	88.52 (3.71–871.28)	0.644

f – fraction; miR – microRNA; IDH – isocitrate dehydrogenase; GB – glioblastoma; NOS – not otherwise specified; RT – radiotherapy; TMZ – temozolomide

The results showed no statistically significant difference in the expression levels of miR-10b/21/34a between the two groups ($p > 0.05$).

DISCUSSION

Given the established role of IDH mutations in glioblastoma and the overexpression of certain oncomiRs and tumor suppressor miRNAs in glioblastoma cells, we investigated the potential association between miR-10b/21/34a expression levels in PBMCs and IDH1 mutation status.

We hypothesized that expression levels of miR-10b, -21, and -34a would positively or negatively correlate with IDH1-mutation status in glioblastoma. Ji et al. [10] found that expression levels of miR-10b progressively rise with the advancement of WHO grades. Considering that miR-21 is a potent oncogene overexpressed in glioblastoma and that glioblastoma cells depend on miR-10b (with the ablation of the miR-10 gene being lethal for these cells) [11], we expected significantly higher expression of miR-10b/21 in the IDH1-wildtype glioblastoma group than in the IDH1-mutant + NOS group. However, our study did not find a statistically significant association between miR-10b/21 expression levels and IDH1 mutation status. On the other hand, Wang et al. [12] proposed an IDH1 mutation-specific miRNA signature. Precisely, in glioblastoma samples, the expression levels of 23 miRNAs varied by more than 1.5-fold between those with mutant IDH1 and those with wild-type IDH1, respectively [12]. One of the microRNAs with aberrant expression in IDH1 mutation glioblastoma is miR-34a. Similar to miR-10b/21 and IDH1-wildtype, we did not find significantly higher levels in the IDH1-mutant + NOS group compared to the IDH1-wildtype group. To check if there is a change in expression levels of miR-10b/21/34a during RT with TMZ in terms of IDH1 mutation status, we investigated and compared expression levels at the 15th and 30th fractions of RT with TMZ, but we did not find statistically significant results as well.

In low-grade glioma (LGG), IDH1/2 mutation status significantly influences miRNA expression [13]. The researchers developed a four-miRNA-based classifier (including miR-10b, -130b, -1304, and -302b) that effectively differentiated between high and low risk for poor prognosis in IDH1/2-mutant LGG [13]. Additionally, one study revealed a trio of miRNAs (miR-1-3p, miR-26a-1-3p, and miR-487b-3p) that showed differential expression in the serum of glioma patients, dependent on their IDH mutation status [14]. The expression and release of these miRNAs were lower in IDH-wildtype glioma cells compared to IDH-mutant cells [14].

Taking into account the previous data from the literature, we tried to understand the results we obtained and why they did not completely match the results from the literature. Despite some differences in the study's design, to the best of our knowledge, direct studies linking miR-10b/21/34a and IDH1 mutation status are limited. However, in the abstract published in 2014, Silber et al. [15] indicate that IDH mutations in gliomas lead to the repression of miR-34a, which is associated with enhanced platelet-derived growth factor (PDGF) signaling. Their findings suggest that miR-34a plays a crucial role in the cellular changes induced by IDH mutations, impacting tumor progression and potential therapeutic strategies [15].

MiRNAs play a vital role in complex regulatory networks that connect numerous genes and pathways, and their expression can be influenced by a variety of factors, making it difficult to establish a direct correlation with a specific mutation such as IDH1-mutation. Glioblastomas are highly heterogeneous tumors, meaning that different regions of the same tumor can have varying genetic and epigenetic profiles. The presence of an IDH1 mutation may trigger compensatory mechanisms within the tumor cells, which could mitigate the impact of the mutation on miRNA expression. Also, although IDH mutations may be the earliest steps in glioma genesis, it is highly likely that other simultaneous or subsequent molecular events are required for further tumor progression, primarily during the transformation of LGGs into HGGs [16]. The glioma microenvironment, various immune cells, stromal elements, and the cytoskeleton can trigger pathways and alter miRNA expression. It is important to emphasize that in our study, we collected samples for microRNA analysis after surgery and prior to starting RT, which may impact our findings. Additionally, the precision of these results might not match those obtained directly from glioblastoma or cerebrospinal fluid samples. Nevertheless, even with complete resection, in glioblastoma, there can be no real complete removal of all tumor cells due to its infiltrative behavior [17]. The tumor cells are considered to be located or migrated in the surrounding brain parenchyma after surgery [18], as well as glioma stem cells responsible for recurrence [19], which suggests that residual tumor cells can still express a spectrum of miRNAs.

It's also worth mentioning that miR-10b and -21 are not the only significant microRNAs in gliomagenesis. There is a spectrum of microRNAs with potential roles as oncomiRs or tumor suppressors. For example, Sippl et al. [20] suggested that miR-181a2 may serve as a prognostic marker for certain patients with IDH1-wildtype glioblastoma. Given that miR-181a2 regulates IDH1 expression in adipose tissue and considering the impact of IDH1 mutation on glioblastoma's clinical course and biological behavior, the researchers investigated the possible influence of miR-181a2 expression levels on IDH expression, the clinical course, and prognosis of GB patients [20]. More precisely, their findings suggest that low expression of miR-181a2 may positively influence the survival of glioblastoma patients through IDH1 regulation [20]. In LGG, Bondarev et al. [21] implied that certain miRNAs, such as miR-182, -455, and -891a, were generally increased in IDH-mutant gliomas, which are associated with a negative prognosis.

Besides the previously mentioned blood sampling after surgery we conducted, another difficulty that can be a limitation of the study is the number of patients included. Increasing the number of patients and samples for microRNA analysis could potentially show a different result. In our study, patients were classified according to the 2016 World Health Organization Classification of Tumors of the Central Nervous System, which in this particular study should not represent an obstacle. Despite a slight difference in prognosis, glioblastoma and diffuse astrocytoma grade IV have low survival rates, indicating that this design of the study could be applied to HGGs as well.

Results from this study are part of the doctoral dissertation of the first author, and represent a continuous work in the field of translational research in the field of radiobiology and a continuation of previously published work on miRNAs in glioblastoma [22, 23].

CONCLUSION

Our study did not confirm the significant correlation of microRNAs-10b/21/34a with IDH1 mutation status. Based on the results, it can be concluded that the expression levels of microRNAs miR-10b, miR-21, and miR-34a do not significantly differ between glioblastoma patients with IDH1-wildtype and those with IDH1-mutant + NOS. These results suggest that the IDH1 mutation status may not be a critical factor for altered expression of miRNA-10b/21/34a in glioblastoma patients. However, further research is encouraged. Identifying a possible association between specific miRNAs and IDH1 mutation status and other clinical and pathological parameters could refine our understanding of HGGs.

ACKNOWLEDGEMENT

Results from this study are part of the results of the doctoral dissertation of the first author Aleksandar Stepanović, PhD (Stepanović A. Association between microRNAs and clinical parameters and response to radiotherapy combined with temozolomide in patients with glioblastoma [dissertation]. Belgrade (Serbia) Faculty of Medicine: University of Belgrade; 2023) under the mentorship of Professor Marina Nikitović, PhD and Senior Research Associate Nina Petrović, PhD.

Conflict of interest: None declared.

REFERENCES

1. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol. 2016;131(6):803–20. [DOI: 10.1007/s00401-016-1545-1] [PMID: 27157931]
2. Louis DN, Perry A, Wesseling P, Brat DJ, Cree IA, Figarella-Branger D, et al. The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. Neuro Oncol. 2021;23(8):1231–51. [DOI: 10.1093/neuonc/noab106] [PMID: 34185076]
3. Ni Y, Shen P, Wang X, Liu H, Luo H, Han X. The Roles of IDH1 in Tumor Metabolism and Immunity. Future Oncol. 2022;18(35):3941–53. [DOI: 10.2217/fon-2022-0583] [PMID: 36621781]
4. Watanabe T, Nobusawa S, Kleihues P, Ohgaki H. IDH1 Mutations Are Early Events in the Development of Astrocytomas and Oligodendrogliomas. Am J Pathol. 2009;174(4):1149–53. [DOI: 10.2353/ajpath.2009.080958] [PMID: 19246647]
5. Gulyaeva LF, Kushlinskiy NE. Regulatory mechanisms of microRNA expression. J Transl Med. 2016;14(1):143. [DOI: 10.1186/s12967-016-0893-x] [PMID: 27197967]
6. Chen B, Li H, Zeng X, Yang P, Liu X, Zhao X, et al. Roles of microRNA on cancer cell metabolism. J Transl Med. 2012;10(1):228. [DOI: 10.1186/1479-5876-10-228] [PMID: 23164426]
7. Zhao H, Meng L, Du P, Liao X, Mo X, Gong M, et al. IDH1 mutation produces R-2-hydroxyglutarate (R-2HG) and induces mir-182-5p expression to regulate cell cycle and tumor formation in glioma. Biol Res. 2024;57(1):30. [DOI: 10.1186/s40659-024-00512-2] [PMID: 38760850]
8. Chen M, Medarova Z, Moore A. Role of microRNAs in glioblastoma. Oncotarget. 2021;12(17):1707–23. [DOI: 10.18632/oncotarget.28039] [PMID: 34434499]
9. O'Brien J, Hayder H, Zayed Y, Peng C. Overview of MicroRNA Biogenesis, Mechanisms of Actions, and Circulation. Front Endocrinol (Lausanne). 2018;9:402. [DOI: 10.3389/fendo.2018.00402] [PMID: 30123182]
10. Ji Y, Wei Y, Wang J, Gong K, Zhang Y, Zuo H. Correlation of microRNA-10b upregulation and poor prognosis in human gliomas. Tumour Biol. 2015;36(8):6249–54. [DOI: 10.1007/s13277-015-3310-9] [PMID: 25773393]
11. El Fatimy R, Subramanian S, Uhlmann EJ, Krichevsky AM. Genome Editing Reveals Glioblastoma Addiction to MicroRNA-10b. Mol Ther. 2017;25(2):368–78. [DOI: 10.1016/j.ymthe.2016.11.004] [PMID: 28153089]
12. Wang Z, Bao Z, Yan W, You G, Wang Y, Li X, et al. Isocitrate dehydrogenase 1 (IDH1) mutation-specific microRNA signature predicts favorable prognosis in glioblastoma patients with IDH1 wild type. J Exp Clin Cancer Res. 2013;32(1):59. [DOI: 10.1186/1756-9966-32-59] [PMID: 23988086]
13. Cheng W, Ren X, Zhang C, Han S, Wu A. Expression and prognostic value of microRNAs in lower-grade glioma depends on IDH1/2 status. J Neurooncol. 2017;132(2):207–18. [DOI: 10.1007/s11060-016-2368-6] [PMID: 28091987]
14. Díaz Méndez AB, Sacconi A, Tremante E, Lulli V, Caprara V, Rosanò L, et al. A diagnostic circulating miRNA signature as orchestrator of cell invasion via TKS4/TKS5/EFHD2 modulation in human gliomas. J Exp Clin Cancer Res. 2023;42(1):66. [DOI: 10.1186/s13046-023-02639-8] [PMID: 36932446]

15. Silber J, Harinath G, Parthasarathy TP, Fabius AWM, Turcan S, Chan TA, et al. Glioma-associated IDH mutation induces miR-34a repression and stem cell-like physiology through enhanced PDGF signaling [abstract]. In: Proceedings of the 105th Annual Meeting of the American Association for Cancer Research; 2014 Apr 5–9; San Diego, CA. Philadelphia (PA): AACR; Cancer Res 2014;74(19 Suppl):Abstract nr 521. [DOI: 10.1158/1538-7445.AM2014-521]
16. Zhang C, Moore LM, Li X, Yung WKA, Zhang W. IDH1/2 mutations target a key hallmark of cancer by deregulating cellular metabolism in glioma. Neuro Oncol. 2013;15(9):1114–26. [DOI: 10.1093/neuonc/not087] [PMID: 23877318]
17. Gerritsen JKW, Broekman MLD, De Vleeschouwer S, Schucht P, Nahed BV, Berger MS, et al. Safe surgery for glioblastoma: Recent advances and modern challenges. Neuro Oncol Pract. 2022;9(5):364–79. [DOI: 10.1093/nop/npac019] [PMID: 36127890]
18. Wei R, Zhou J, Bui B, Liu X. Glioma actively orchestrate a self-advantageous extracellular matrix to promote recurrence and progression. BMC Cancer. 2024;24(1):974. [DOI: 10.1186/s12885-024-12751-3] [PMID: 39118096]
19. Chen C, Jing W, Chen Y, Wang G, Abdalla M, Gao L, et al. Intracavity generation of glioma stem cell–specific CAR macrophages primes locoregional immunity for postoperative glioblastoma therapy. Sci Transl Med. 2022;14(656):eabn1128. [DOI: 10.1126/scitranslmed.abn1128] [PMID: 35921473]
20. Sippl C, Schoeneberger L, Teping F, Schulz-Schaeffer W, Urbschat S, Ketter R, et al. Impact of MiRNA-181a2 on the Clinical Course of IDH1 Wild Type Glioblastoma. Processes. 2021;9(5):728. [DOI: 10.3390/pr9050728]
21. Bondarev AA, Evpak AS, Novoselov AL, Kudriaeva AA, Belogurov AA Jr. The Correlation Patterns of miRNA Expression with Targeted mRNA Transcripts in Glioma Patients with Wild-Type and Mutated Isocitrate Dehydrogenase (IDH) Genotypes. Acta Naturae. 2024;16(3):38–45. [DOI: 10.32607/actanaturae.27363] [PMID: 39539523]
22. Nikitovic M, Stanojkovic T. Current aspects of radiobiology in modern radiotherapy – our clinical experience. Srp Arh Celok Lek. 2022;150(11–12):732–36. [DOI: 10.2298/SARH220131085N]
23. Stepanović A, Nikitović M, Stanojković TP, Grujičić D, Bukumirić Z, Srbljak I, et al. Association between microRNAs 10b/21/34a and acute toxicity in glioblastoma patients treated with radiotherapy and temozolomide. Sci Rep. 2022;12(1):7505. [DOI: 10.1038/s41598-022-11445-9] [PMID: 35525840]

Корелација нивоа експресије микроРНК-10б/21/34а са мутационим статусом *IDH1* код болесника са глиобластомом

Александар Степановић[1,2], Нина Петровић[3,4], Татјана Арсенијевић[1,2], Марина Никитовић[1,2]

[1]Универзитет у Београду, Медицински факултет, Београд, Србија;
[2]Институт за онкологију и радиологију Србије, Клиника за радијациону онкологију, Београд, Србија;
[3]Институт за онкологију и радиологију Србије, Одељење за експерименталну онкологију, Београд, Србија;
[4]Универзитет у Београду, Институт за нуклеарне науке „Винча" – Национални институт Републике Србије, Београд, Србија

САЖЕТАК

Увод/Циљ Мутације изоцитрат дехидрогеназе (ИДХ) играју значајну улогу у глиомагенези. Поједине микроРНК као што су микроРНК-10б/21 делују као онкогене микроРНК, док микроРНК-34а делује као тумор супресор код глиобластома. Наша студија је имала за циљ да истражи потенцијалну корелацију статуса мутације ИДХ1 са нивоима експресије микроРНК-10б/21/34а код пацијената са глиобластомом.

Методе Ова студија је обухватила 43 пацијента који су имали постављену дијагнозу глиобластома. Испитивани су нивое експресије микроРНК-10б, микроРНК-21 и микроРНК-34а у мононуклеарним ћелијама периферне крви након операције, односно пре почетка лечења радиотерапијом са конкомитантним темозоломидом, као и на 15. и 30. фракцији радиотерапије са конкомитантним темозоломидом. Подаци о статусу мутације ИДХ1 прикупљени су из историје болести и дефинитивног хистопатолошког налаза.

Резултати Направљене су две групе за процену корелације нивоа експресије микроРНК-10б/21/34а у односу на ИДХ1 мутациони статус: глиобластом ИДХ1-дивљи тип и глиобластом ИДХ1-мутант + *Not Otherwise Specified* (*NOS*). Медијана експресије микроРНК-10б пре почетка конкоминатног лечења радиохемиотерапијом била је 130,44 (52,2–622,53) у групи ИДХ1-дивљег типа глиобластома и 94,61 (2,13–816,89) у групи ИДХ1-мутант + *NOS*. Медијана експресије микро РНК-21 била је 57,16 (2,68–278,98) у групи глиобластома ИДХ1 дивљег типа и 69,74 (4,6–825,43) у групи ИДХ1-мутант + *NOS*. Медијана експресије микроРНК-34а била је 13,52 (3,16–105,2) у групи глиобластома ИДХ1 дивљег типа и 10,11 (1–210,55) у групи ИДХ1-мутант + *NOS*. Није доказана статистички значајна разлика у нивоима експресије микроРНК-10б/21/34а између две посматране групе ($p > 0,05$).

Закључак. Наши резултати сугеришу да статус мутације ИДХ1 можда није кључни фактор за измењену експресију микроРНК-10б/21/34а код пацијената са глиобластомом.

Кључне речи: глиобластом; микроРНК; ИДХ мутација