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ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

Relation of oncogenic microRNA-10b and microRNA-21 to glioblastoma size and localization

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SUMMARY

Introduction/Objective In glioblastoma, upregulation of oncogenic microRNA-10b (miR-10b) and microRNA-21 (miR-21) is often found. Our study aimed to investigate whether there is a link between miR-10b and miR-21 expression levels and tumor size and tumor localization.

Methods The research involved 43 patients diagnosed with glioblastoma. We analyzed the expression levels of miR-10b and miR-21 post-surgery. The data on tumor size and tumor localization were obtained from magnetic resonance imaging.

Results The median expression level of miR-10b in patients with tumors < 4 cm was 214.86 (min–max: 2.13–816.89), while in patients with tumors ≥ 4 cm, the median expression level was 92.99 (min–max: 19.24–491.82). The median expression level of miR-21 in patients with tumors < 4 cm was 81.69 (min–max: 11.39–825.43), whereas in patients with tumors ≥ 4 cm, the median expression level was 40.84 (min–max: 2.68–278.98). For both miR-10b and miR-21, a statistically significant difference was found for tumors < 4 cm ($p = 0.027$ and $p = 0.047$, respectively) compared to those ≥ 4 cm. There was no statistically significant difference in the expression levels of miR-10b ($p = 0.675$) and miR-21 ($p = 0.183$) in relation to tumor localization.

Conclusion Glioblastomas smaller than 4 cm have statistically significantly higher expression levels of miR-10b and miR-21 compared to glioblastomas equal to or larger than 4 cm. Although this result is unexpected, it could mean that miR expression levels dynamically change after surgery and according to the altered microenvironment.

Keywords: glioblastoma; microRNA; tumor size

INTRODUCTION

Tumor histology, tumor size, grade, vascular invasion, stage and other clinicopathological and molecular features are often described as prognostic factors in patients with extracranial cancer [1, 2]. For patients diagnosed with malignant intracranial tumors such as glioblastoma, the most reliable prognostic factors are age, O6-methylguanine-DNA methyltransferase (MGMT) promoter methylation, isocitrate dehydrogenase (IDH) mutation, extent of surgical resection and tumor location [3, 4]. The size of the tumor in patients with glioblastoma has also been shown to be a possible prognostic factor for survival [3, 5, 6].

MicroRNA-10b (miR-10b) and microRNA-21 (miR-21) are amongst the most researched microRNAs in human oncology. They are often overexpressed in a spectrum of human cancers. MiR-21 is frequently overexpressed in various cancers, including glioblastoma [7]. Due to the hypoxic conditions present in glioblastoma cells, an upregulation of miR-10b/miR-21 can be observed [8].

miR-10b is recognized as a potent oncogenic microRNA (oncomiR) involved in the regulation of the cell cycle. Upregulation of miR-10b can promote tumor growth, invasion and migration [9]. Through diversiform gene regulation and signaling pathways, overexpression of miR-21 is shown to play an important role in oncogenesis and tumor metastasis, as well as in resistance to oncologic treatment [10]. In glioblastoma, miR-21 is upregulated and thus, often linked with tumor pathogenesis, as well as radioresistance and chemotherapy resistance [7]. Both miR-10b and miR-21 are shown to be associated with clinical and pathologic features such as tumor size [11], disease stage, and metastatic lymph nodes in extracranial tumors [12].

Inhibition of tumor growth and glioblastoma cell proliferation has been demonstrated in *in vitro* and *in vivo* experiments in gliomas [13] and glioblastoma [14] by knocking down microRNAs, such as miR-10b [15] and miR-21 [13, 14]. However, the level of their expression in body fluids and the possible association with glioblastoma features, such as tumor size and tumor location, remains less clear.

Our study aimed to investigate whether there is an association between the expression levels of miR-10b and miR-21 and the tumor

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size and its localization in patients diagnosed with glioblastoma.

METHODS

This prospective cohort study followed forty-three glioblastoma patients who had undergone surgery and were about to start treatment with Stupp regimen [16]. The research focused on the levels of two specific miRNAs, miR-10b and miR-21, extracted from the patients' peripheral blood mononuclear cells (PBMCs). These patients were treated at the Clinic of Neurosurgery and the Neuro-Oncology Department at the University Clinical Center of Serbia, as well as the Institute for Oncology and Radiology of Serbia, starting in October 2017.

The study gathered clinical parameters, focusing on tumor size (< 4 cm and ≥ 4 cm) and tumor location (frontal lobe, temporal lobe, parietal lobe, occipital lobe, thalamus, or multilobar). Clinical data on tumor size and location were obtained from medical records, specifically magnetic resonance imaging (MRI).

PBMCs were isolated from heparinized whole blood through centrifugation at 4°C using Histopaque-1077, following the manufacturer's instructions. miRNA molecules were extracted and purified from PBMCs using TRI Reagent, as per the manufacturer's protocol. The RNA samples were quantified using a BioSpec-nano spectrophotometer (Shimadzu Corporation, Kyoto, Japan), with samples having an A260/280 ratio between 1.7 and 2.1 considered suitable for further analysis. To analyze miR-10b and miR-21, specific TaqMan® MicroRNA assays and the TaqMan® MicroRNA Reverse Transcription Kit were used. Starting with 10 ng of total RNA for reverse transcription, the cDNA was then amplified using TaqMan™ Universal Master Mix II on a 7500 Real-Time PCR System (Applied Biosystems, Foster City, CA, USA). Relative quantities (RQ) were calculated using the comparative delta-delta Ct method, normalizing all samples to the endogenous control RNU6B and calibrating to the sample with the lowest RQ value.

Statistical analysis

To compare differences between two separate groups, we utilized the Mann-Whitney U test. For analyzing the correlation between miRNA expression levels and clinical parameters, we employed both Pearson and Spearman tests. The Kruskal Wallis test was used for comparing three groups. The Log-Rank (Mantel–Cox) test was used to determine the significance of differences. All statistical analyses were performed using IBM SPSS Statistics, Version 22.0 (IBM Corp., Armonk, NY, USA).

Ethics

All participants gave their informed consent, and the study complied with the ethical guidelines of the Declaration of Helsinki. The Ethical Research Committee at the Faculty of Medicine, University of Belgrade, reviewed and approved the study protocol under the reference number 1322/X-39.

RESULTS

In this study, we examined the correlation between the expression levels of miR-10b and miR-21 and the data on tumor size and tumor location in 43 patients with glioblastoma, using 43 samples for each microRNA molecule.

Most patients had a tumor located in the temporal lobe (34.9%), while both multifocal and thalamic tumor were present in 2.3% of the patients. Tumor ≥ 4 cm was observed in 62.8% of the patients. The clinical features are presented in Table 1.

Table 1. Data on tumor location and tumor size of patients with glioblastoma

Tumor location	No (%)
Frontal lobe	14 (32.6%)
Temporal lobe	15 (34.9%)
Parietal lobe	10 (23.3%)
Occipital lobe	2 (4.7%)
Multifocal tumor	1 (2.3%)
Thalamic tumor	1 (2.3%)
Tumor size	No (%)
< 4 cm	16 (37.2%)
≥ 4 cm	27 (62.8%)

The association between miR-10b and miR-21 expression levels and tumor size (< 4 cm and ≥ 4 cm) was investigated. The median expression level of miR-10b in patients with tumors smaller than 4 cm was 214.86 (range: 2.13–816.89), while in patients with tumors ≥ 4 cm, the median expression level was 92.99 (range: 19.24–491.82). For miR-10b, a statistically significant difference was found for tumors smaller than 4 cm ($p = 0.027$). The median expression level of miR-21 in patients with tumors smaller than 4 cm was 81.69 (range: 11.39–825.43), whereas in patients with tumors ≥ 4 cm, the median expression level was 40.84 (range: 2.68–278.98). A statistically significant difference was also found for miR-21 in tumors smaller than 4 cm ($p = 0.047$) compared to tumors ≥ 4 cm.

Due to the unfavorable ratio of the number of different tumor localizations (frontal lobe – 14 patients, temporal lobe – 15 patients, parietal lobe – 10 patients, occipital lobe – two patients, multilobar tumor – one patient, thalamus – one patient) and potential predictors, it was not possible to make a comparison for each localization separately. Instead, according to data from the literature, three groups were created to compare tumor localization with miR-10b and miR-21 expression levels: tumors in the frontal lobe (frontal), tumors in the temporal lobe (temporal), and tumors in other lobes (Figures 1 and 2). The results showed that there was no statistically significant difference in the expression levels of miR-10b ($p = 0.675$) and miR-21 ($p = 0.183$) in relation to tumor localization (Table 2) (Figures 1 and 2).

Table 2. MicroRNA-10b and microRNA-21 expression levels and tumor localization

MicroRNA	Median (range)	p-value
microRNA-10b		
Frontal lobe	153.23 (2.13–622.53)	0.675
Temporal lobe	92.99 (41.18–816.89)	
Other lobes	102.18 (30.09–465.62)	
microRNA-21		
Frontal lobe	81.69 (11.42–825.43)	0.183
Temporal lobe	53.48 (2.68–706.23)	
Other lobes	35.70 (5.82–278.98)	

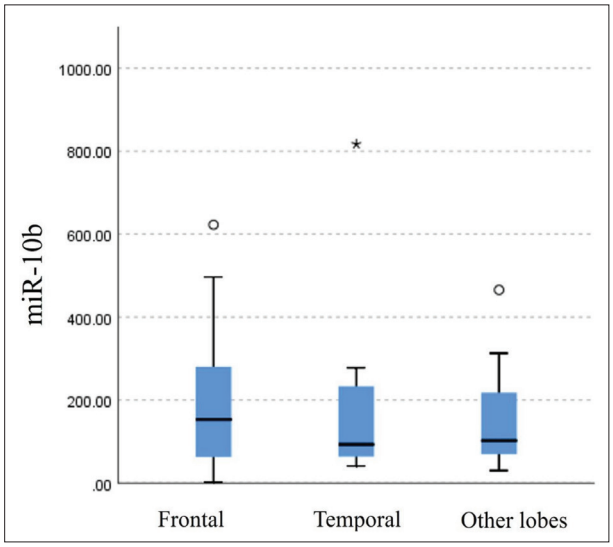

Figure 1. Comparison of median expression levels of microRNA-10b in the frontal, temporal, and other lobes where glioblastoma is diagnosed

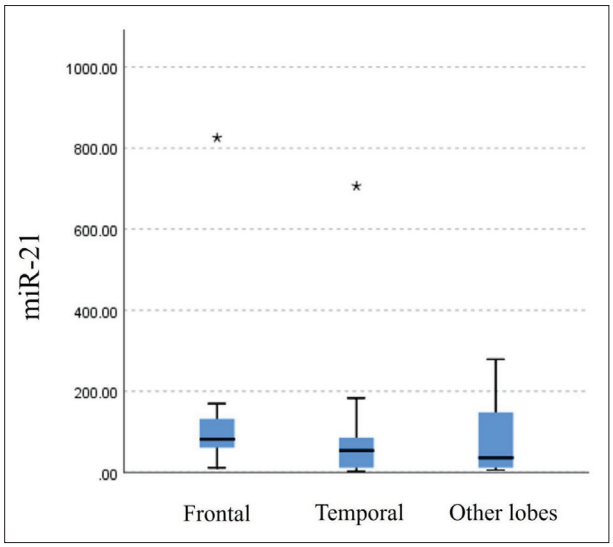

Figure 2. Comparison of median expression levels of microRNA-21 in the frontal, temporal, and other lobes where glioblastoma is diagnosed

DISCUSSION

Our study aimed to determine whether there is a link between the expression levels of miR-10b and miR-21 and clinicopathological factors such as tumor size and localization.

Scientific studies on glioblastoma often classify tumors into two categories based on size: those measuring < 4 cm and those measuring ≥ 4 cm. However, the rationale for selecting this specific size as a benchmark is not clearly established. The debate on this matter frequently involves questions about whether 4 cm represents the size at which tumors are most commonly diagnosed – namely, when patients exhibit symptoms prompting diagnostic procedures – or whether this threshold impacts the extent of surgical resection, the success of adjuvant therapies, and the overall prognosis of the disease. Upon review of the literature and the data presented, we decided to utilize a tumor size of 4 cm as the reference value in this study. Statistical significance was found only for the expression levels of miR-10b and miR-21 in tumors smaller than 4 cm, which was unexpected. We had formed a hypothesis that the expression levels of miR-10b and miR-21 would be statistically significant in tumors larger than 4 cm.

MiR-21 is recognized as one of the most potent oncogenes, playing a pivotal role in carcinogenesis, metastatic potential, and disease relapse [17]. This observation led us to hypothesize that larger tumors at the time of disease presentation may exhibit higher expression levels of miR-21. Supporting this hypothesis, we noted that overexpression of miR-21 was identified in breast tumor tissue, and using a miR-21 inhibitor, known as antimiR-21, inhibited tumor cell growth both *in vitro* and *in vivo* [18]. Furthermore, miR-21 is also one of the most upregulated microRNAs in glioblastoma, and studies demonstrated that knocking down miR-21 in glioblastoma cells resulted in reduced cell growth [19]. On the other hand, miR-10b is regarded as a highly oncogenic microRNA, with its overexpression observed in glioblastoma, influencing tumorigenesis, or gliomagenesis [20]. Ji et al. [21] investigated the association between miR-10b expression levels and prognosis in patients with glioma. They found that there is a higher expression level of miR-10b in glioma patients compared to normal brain parenchyma. Also, upregulation of miR-10b in glioma was correlated with higher glioma grade and larger tumor size [21]. Regarding glioblastoma size and microRNA expression, Siegal et al. [22] reported that in the group of patients with glioblastoma who were treated with bevacizumab, there was a significant negative correlation between miR-10b and miR-21 levels and changes in tumor diameters. The authors revealed that they used serum for the determination of expression levels of specific microRNAs. Moderately analogous to the previously mentioned study, in our study, we investigated microRNA expression levels from patients' plasma and measured tumor size by MRI, as well.

Glioblastoma is an infiltrative tumor, and glioma stem cells could be in the area of the cavity or in the remaining tumor after partial resection, which could be responsible for different microRNA expression levels. Nevertheless, for accurate interpretation of microRNA expression levels and their association with tumor size, it could be essential to measure microRNA levels before any surgical treatment and compare them not only to the MRI size of the tumor, but to the actual size of the tumor after surgery. In our

study, we measured these levels after surgery and before the start of radiotherapy with temozolomide, which could affect the results. However, when it comes to glioblastomas, which are known for their heterogeneous pathological features, including varying foci and sizes of necrosis, smaller tumors might show less pronounced necrotic areas. This means that the microenvironment of glioblastoma and the surrounding tissue, as well as intracellular and intercellular communication, might not be completely disrupted. That might imply that even smaller tumors could show microRNA overexpression and exhibit a higher proliferative capacity. In most cases, for extracranial tumors, the proportion of tumor necrosis is often associated with tumor size [23]. Regarding glioblastoma, the interpretation of the connection between tumor size and tumor necrosis size may be difficult. Some studies reveal that even a small glioblastoma can have various extents of necrosis, and conversely [24]. Moreover, due to the complexity of glioblastoma microenvironment in terms of the possibility of glioblastoma and glioblastoma stem cells reprogramming their microenvironment [25], different microenvironments may affect microRNA expression, especially after surgery. When interpreting microRNA expression levels, it's important to consider how microRNAs are released, the ability of cells to release them, and what tissue is used for the determination of their expression levels. Although the exact mechanism of microRNA release is not fully understood, data suggests that microRNAs are released from both apoptotic bodies and viable tumor cells. Intercellular communication involving microRNAs occurs through exosomes, extracellular vesicles, and other pathways [26]. It also should be borne in mind that in the human brain, the only cells that could express miR-10b are human brain microvascular endothelial cells [27], which could affect the results as well.

Bearing in mind data from the literature on the different expressions of specific microRNAs in the corresponding parts of the brain, we investigated whether there is a difference between the expression level of miR-10b and miR-21 in relation to the localization of the tumor. However, we did not find statistical significance in the expression level of miR-10b and miR-21 between tumors in the frontal lobe, temporal lobe, and tumors in other localizations. To the best of our knowledge, there is not a study that compares the expression level of miR-10b and miR-21 in relation to the localization of glioblastoma in different brain lobes. However, we found another research on a similar topic. Among other results, Ozdogan et al. [28] did not find a significant correlation between the expression level of miR-221 and glioma localization in the brain.

We considered that the main limitations of our study were (1) collecting samples after surgery and (2) tumor size measurements that were noted only in the MRI. On the other hand, these limitations could also lead to more research on the different dynamic changes in microRNA profiles after surgery and the possible influence of the microenvironment or treatment on tumor size and microRNA expression profiles, respectively.

Given that PBMCs are a minimally invasive and easily accessible source of microRNAs, we isolated miRNAs from patients' PBMCs with glioblastoma in our study. Nevertheless, some studies acknowledge that miRNA values may differ between PBMCs and whole blood [29]. The results of our study would be even more precise if the miRNA values isolated from PBMCs were compared with those from whole blood or even tumor tissue.

Results of this paper are part of the doctoral dissertation of the second author of the paper, and are part of the translational research from the radiobiology team of our institute [30].

CONCLUSION

Tumors smaller than 4 cm have statistically significantly higher expression levels of miR-10b and miR-21 compared to glioblastomas equal to or larger than 4 cm. Although this result is unexpected, it could mean that microRNA expression levels dynamically change after surgery and with the altered microenvironment. There was no statistical significance in the expression levels of miR-10b and miR-21 between tumors in the frontal lobe, temporal lobe, and tumors in other localizations.

Considering all the functions microRNAs possess in normal cells and tumor cells, further research on glioblastoma microRNA profiles is needed. Elucidation of the mechanisms of gliomagenesis and tumor growth in relation to the expression profile of specific microRNAs is important in the future for developing potential diagnostic methods using liquid biopsies or new therapeutic strategies.

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Only part of the results was presented in poster form at the 1st Net4Brain Annual Meeting: Closing the translational gap in brain cancer treatment, Ljubljana, Slovenia, 4th–6th September 2024, under the title "Correlation of microRNAs-10b/21 expression levels and tumor size in patients with glioblastoma."

Conflict of interest: None declared.

REFERENCES

1. Shao Y, Yu Y, Luo Z, Guan H, Zhu F, He Y, et al. Clinical, Pathological Complete Response, and Prognosis Characteristics of HER2-Low Breast Cancer in the Neoadjuvant Chemotherapy Setting: A Retrospective Analysis. Ann Surg Oncol. 2022;29(13):8026–34. [DOI: 10.1245/s10434-022-12369-4] [PMID: 35933542]
2. Abdel-Razeq H, Iweir S, Abdel-Razeq R, Rahman FA, Almasri H, Bater R, et al. Differences in clinicopathological characteristics, treatment, and survival outcomes between older and younger breast cancer patients. Sci Rep. 2021;11(1):14340. [DOI: 10.1038/s41598-021-93676-w] [PMID: 34253800]
3. Șerban G, Tămaș F, Bălașa R, Manu D, Tămaș C, Bălașa A. Prognostic Factors of Survival in Glioblastoma Multiforme Patients—A Retrospective Study. Diagnostics. 2022;12(11):2630. [DOI: 10.3390/diagnostics12112630] [PMID: 36359474]
4. Brown NF, Ottaviani D, Tazare J, Gregson J, Kitchen N, Brandner S, et al. Survival Outcomes and Prognostic Factors in Glioblastoma. Cancers. 2022;14(13):3161. [DOI: 10.3390/cancers14133161] [PMID: 35804940]
5. Leu S, Boulay JL, Thommen S, Bucher HC, Stippich C, Mariani L, et al. Preoperative Two-Dimensional Size of Glioblastoma is Associated with Patient Survival. World Neurosurg. 2018;115:e448–63. [DOI: 10.1016/j.wneu.2018.04.067] [PMID: 29678715]
6. Alimohammadi E, Bagheri SR, Sadeghsalehi A, Rizevandi P, Rezaie Z, Abdi A, et al. Prognostic factors in patients with glioblastoma multiforme: focus on the pathologic variants. Acta Neurol Belg. 2020;120(6):1341–50. [DOI: 10.1007/s13760-019-01171-x] [PMID: 31222512]
7. Rhim J, Baek W, Seo Y, Kim JH, Cheon Y, Lee SG, et al. From Molecular Mechanisms to Therapeutics: Understanding MicroRNA-21 in Cancer. Cells. 2022;11(18):2791. [DOI: 10.3390/cells11182791] [PMID: 36139366]
8. Charbit H, Lavon I. Investigating Expression Dynamics of miR-21 and miR-10b in Glioblastoma Cells In Vitro: Insights into Responses to Hypoxia and Secretion Mechanisms. Int J Mol Sci. 2024;25(14):7984. [DOI: 10.3390/ijms25147984] [PMID: 39063226]
9. Pekarek L, Torres-Carranza D, Fraile-Martinez O, García-Montero C, Pekarek T, Saez MA, et al. An Overview of the Role of MicroRNAs on Carcinogenesis: A Focus on Cell Cycle, Angiogenesis and Metastasis. Int J Mol Sci. 2023;24(8):7268. [DOI: 10.3390/ijms24087268] [PMID: 37108432]
10. Hashemi M, Mirdamadi MSA, Talebi Y, Khaniabad N, Banaei G, Daneii P, et al. Pre-clinical and clinical importance of miR-21 in human cancers: Tumorigenesis, therapy response, delivery approaches and targeting agents. Pharmacol Res. 2023;187:106568. [DOI: 10.1016/j.phrs.2022.106568] [PMID: 36423787]
11. Mahmood N, Hanif M, Ahmed A, Jamal Q, Mushtaq S, Khan A, et al. Circulating miR-21 as a prognostic and predictive biomarker in oral squamous cell carcinoma: Circulating miR-21. Pak J Med Sci. 2019;35(5):1408–12. [DOI: 10.12669/pjms.35.5.331] [PMID: 31489016]
12. Zhang J, Yang J, Zhang X, Xu J, Sun Y, Zhang P. MicroRNA-10b expression in breast cancer and its clinical association. Ahmad A, editor. PLoS One. 2018;13(2):e0192509. [DOI: 10.1371/journal.pone.0192509] [PMID: 29408861]
13. Corsten MF, Miranda R, Kasmieh R, Krichevsky AM, Weissleder R, Shah K. MicroRNA-21 Knockdown Disrupts Glioma Growth In vivo and Displays Synergistic Cytotoxicity with Neural Precursor Cell–Delivered S-TRAIL in Human Gliomas. Cancer Res. 2007;67(19):8994–9000. [DOI: 10.1158/0008-5472.CAN-07-1045] [PMID: 17908999]
14. Yang CH, Yue J, Pfeffer SR, Fan M, Paulus E, Hosni-Ahmed A, et al. MicroRNA-21 Promotes Glioblastoma Tumorigenesis by Down-regulating Insulin-like Growth Factor-binding Protein-3 (IGFBP3). J Biol Chem. 2014;289(36):25079–87. [DOI: 10.1074/jbc.M114.593863] [PMID: 25059666]
15. Ma C, Wei F, Xia H, Liu H, Dong X, Zhang Y, et al. MicroRNA-10b mediates TGF-β1-regulated glioblastoma proliferation, migration and epithelial-mesenchymal transition. Int J Oncol. 2017;50(5):1739–48. [DOI: 10.3892/ijo.2017.3947] [PMID: 28393237]
16. Stupp R, Mason WP, van den Bent MJ, Weller M, Fisher B, Taphoorn MJB, et al. Radiotherapy plus Concomitant and Adjuvant Temozolomide for Glioblastoma. N Engl J Med. 2005;352(10):987–96. [DOI: 10.1056/NEJMoa043330] [PMID: 15758009]
17. Liu J, Zhu H, Yang X, Ge Y, Zhang C, Qin Q, et al. MicroRNA-21 is a novel promising target in cancer radiation therapy. Tumour Biol. 2014;35(5):3975–9. [DOI: 10.1007/s13277-014-1623-8] [PMID: 24446181]
18. Si ML, Zhu S, Wu H, Lu Z, Wu F, Mo YY. miR-21-mediated tumor growth. Oncogene. 2007;26(19):2799–803. [DOI: 10.1038/sj.onc.1210083] [PMID: 17072344]
19. Bassot A, Dragic H, Haddad SA, Moindrot L, Odouard S, Corlazzoli F, et al. Identification of a miRNA multi-targeting therapeutic strategy in glioblastoma. Cell Death Dis. 2023;14(9):630. [DOI: 10.1038/s41419-023-06117-z] [PMID: 37749143]
20. Chen M, Medarova Z, Moore A. Role of microRNAs in glioblastoma. Oncotarget. 2021;12(17):1707–23. [DOI: 10.18632/oncotarget.28039] [PMID: 34434499]
21. Ji Y, Wei Y, Wang J, Gong K, Zhang Y, Luo J, et al. 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]
22. Siegal T, Biegel T, Paldor I, Zelikovitch B, Canello T, Benis A, et al. Dynamics of circulating hypoxia-mediated miRNAs and tumor response in patients with high-grade glioma treated with bevacizumab. J Neurosurg. 2016;125(4):1008–15. [DOI: 10.3171/2015.8.JNS15437] [PMID: 26799295]
23. Yee PP, Li W. Tumor necrosis: A synergistic consequence of metabolic stress and inflammation. BioEssays. 2021;43(7):2100029. [DOI: 10.1002/bies.202100029] [PMID: 33998010]
24. Yee PP, Wei Y, Kim SY, Lu T, Chih SY, Lawson C, et al. Neutrophil-induced ferroptosis promotes tumor necrosis in glioblastoma progression. Nat Commun. 2020;11(1):5424. [DOI: 10.1038/s41467-020-19193-y] [PMID: 33110073]
25. Sharma P, Aaroe A, Liang J, Puduvalli VK. Tumor microenvironment in glioblastoma: Current and emerging concepts. Neurooncol Adv. 2023;5(1):vdad009. [DOI: 10.1093/noajnl/vdad009] [PMID: 36968288]
26. Buruiană A, Florian Ștefan I, Florian AI, Timiș TL, Mihu CM, Miclăuș M, et al. The Roles of miRNA in Glioblastoma Tumor Cell Communication: Diplomatic and Aggressive Negotiations. Int J Mol Sci. 2020;21(6):1950. [DOI: 10.3390/ijms21061950] [PMID: 32178454]
27. 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]
28. Ozdogan S, Yaltirik CK, Yilmaz SG, Akdeniz FT, Sumerkent K, Duzkalir AH, et al. Investigation of the Effects of MicroRNA-221 Expression Levels in Glioblastoma Multiforme Tumors. Anticancer Res. 2020;40(6):3265–70. [DOI: 10.21873/anticanres.14308] [PMID: 32487621]
29. Atarod S, Smith H, Dickinson A, Wang XN. MicroRNA levels quantified in whole blood varies from PBMCs. F1000Res. 2014;3:183. [DOI: 10.12688/f1000research.4884.4] [PMID: 26500764]
30. Nikitovic M, Stanojkovic T. Current aspects of radiobiology in modern radiotherapy–our clinical experience. Srp Arh Celok Lek. 2022;150(11–12):732–6. [DOI: 10.2298/SARH220131085N]

Повезаност онкогених микроРНК-10б и микроРНК-21 са величином и локализацијом глиобластома

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САЖЕТАК

Увод/Циљ Код глиобластома често се уочава појачана експресија онкогених микроРНК-10б и микроРНК-21. Циљ наше студије је био да истражи да ли постоји повезаност између нивоа експресије микроРНК-10б/21 и величине и локализације глиобластома.

Методе У истраживању су учествовала 43 болесника са дијагнозом глиобластома. Анализирали смо нивое експресије микроРНК-10б/21 након оперативног лечења. Подаци о величини и локализацији глиобластома добијени на основу налаза магнетне резонанце.

Резултати Медијана експресије микроРНК-10б код болесника са туморима < 4 *cm* износила је 214,86 (опсег: 2,13–816,89), док је код болесника са туморима ≥ 4 *cm* била 92,99 (опсег: 19,24–491,82). Медијана експресије микроРНК-21 код болесника са туморима < 4 *cm* била је 81,69 (опсег: 11,39–825,43), док је код болесника са туморима ≥ 4 *cm* била 40,84 (опсег: 2,68–278,98). За микроРНК-10б и за микроРНК-21 нађена је статистички значајна разлика за туморе < 4 *cm* ($p = 0,027$, односно $p = 0,047$) у поређењу са туморима ≥ 4 *cm*. Није било статистички значајне разлике у нивоима експресије микроРНК-10б ($p = 0,675$) и микроРНК-21 ($p = 0,183$) у односу на локализацију тумора.

Закључак Глиобластоми мањи од 4 *cm* имају статистички значајно веће нивое експресије микроРНК-10б и микроРНК-21 у поређењу са глиобластомима једнаким или већим од 4 *cm*. Иако је овај резултат неочекиван, он може упућивати на то да се нивои експресије микро РНК динамички мењају након операције и у складу са измењеним микроокружењем глиобластома.

Кључне речи: глиобластом; микроРНК; величина тумора