Archives of Advances in Biosciences

Original Article

OPEN ACCESS

Attenuating effect of sialic acid on GD-2 expression under Temozolomide treatment in glioma cell line

Hajar Hoveizavi [1] Hamid Galehdari [2*] , Mehrdad Hashemi [3,4], Alihossein Saberi[5], Masoumeh Heshmati[1]

[1.] Department of Cellular and Molecular Biology, TeMS.C., Islamic Azad University, Tehran, Iran.
[2.] Department of Biology, Faculty of Sciences, Shahid Chamran University of Ahvaz, Ahvaz, Iran. Email: galehdari@scu.ac.ir
[3.] Farhikhtegan Medical Convergent Sciences Research Center, Farhikhtegan hospital., Faculty of medicine.,TeMs. C., Islamic Azad University, Tehran, Iran.
[4.] Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
[5.] Department of Medical Genetics, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Received: 27 Jun 2026; **Accepted:** 05 Sep 2026; **Published:** 14 Oct 2026

Cite this article as: Hoveizavi H, Galehdari H, Hashemi M, Saberi A, Heshmati M. Attenuating effect of sialic acid on GD-2 expression under Temozolomide treatment in glioma cell line. Archives of Advances in Biosciences. 2026 17(1):1-7. https://doi.org/10.22037/aab.v17i1.52614

Abstract

Background and Aim: Targeted therapies have demonstrated promising and safe results in clinical trials. However, due to instances of drug failure, researchers have investigated combinatorial therapies to improve therapeutic outcomes. The presence of hypersialylated tumor cell surfaces promotes abnormal cell trafficking and contributes to drug resistance, yet its mechanistic role in astrocytoma is not fully understood.

In this study, we comparatively evaluated the impact of sialic acid, temozolomide, and their combination on cell viability and apoptosis using IC50 and EC50 values. Additionally, Real-Time PCR was used to analyze GD-2 synthase expression following combined treatment to investigate the underlying reasons for drug failure in combinatorial therapy.

Methods: The values of Inhibitory Concentration (IC50) and Enhanced Concentration (EC50) were determined using the MTT assay, and GD-2 synthase gene expression was evaluated by RT-qPCR across distinct treatment categories.

Results: Sialic acid reduced Temozolomide cytotoxicity and *GD-2* gene expression. Despite the fact that TMZ had no significant effect on GD-2 synthase expression, suggesting no interfering trace on anti-GD2 immunotherapy, the IC50 of TMZ changed in the presence of sialic acid. This alteration may be associated with the development of drug resistance in cancerous cells, which may affect the molecular mechanism of drug failure and the proposed beneficial purpose for targeted therapy to achieve superior therapeutic outcomes.

Conclusion: The present research indicates that sialic acid may promote cancer progression and decreases the effectiveness of anticancer drugs, including chemotherapy and GD2 antigen expression, and has the potential to reduce the effectiveness of anti-*GD2*-based immunotherapy. Hence, considering sialic acid levels or its biosynthesis within a multimodal therapeutic framework may serve as an effective strategy to mitigate its adverse impact on treatment outcomes.

Keywords: Sialic Acid; Temozolomide; glioma cell line; GD-2 antigen; immunotherapy.

1. Introduction

Astrocytoma is an aggressive type of central nervous system tumor with a high mortality and morbidity rate (1). Grade 2 tumors are known as diffuse astrocytomas, which account for almost 15 to 20 percent of glial tumors throughout the central nervous

This open-access article distributed under the terms of the Creative Commons Attribution- Noncommercial 4.0 International License

system, with a median survival of approximately 7-8 years (2, 3). Recent research has indicated that 74% of low-grade astrocytomas (LGG) turn into glioblastoma multiforme (GBM), referred to as the secondary form of glioma, which has a median survival of less than one year (2).

Despite the advancements in cancer therapy, encompassing various modalities such as surgery, chemotherapy, radiotherapy, hormonal therapy, targeted therapy, and biological treatments, it is still difficult to treat glioma due to various reasons (4, 5). Various studies have identified several factors associated with the LGG's malignant transformation. A groundbreaking study by a multidisciplinary team revealed that temozolomide might be involved in LGGs MT (6). Temozolomide chemotherapy is considered to be the initial choice for the treatment of glioma, often used following surgery and radiotherapy (7, 8), and it is introduced as a valid option for the treatment of LGGs (9). However, it has several significant side effects and, as mentioned above, might be involved in LGG MT (6).

Immunotherapy is a promising approach to glioma treatment (10, 11). The GD-2 antigen was initially introduced for immunotherapy of neuroblastoma (12-14). However, recent research has demonstrated that since GBM cells express GD2, it can be used as an immunotherapy approach for glioma treatment (15).

The emergence of drug resistance represents a fundamental hallmark that promotes cancer cell persistence, posing a formidable threat to the global healthcare system. Alterations in sialyltransferase (ST) expression can lead to hypersialylation, which is a well-documented feature of malignancy. Aberrant sialylation profile is a key driver of therapeutic evasion, as it facilitates resistance to both targeted and conventional modalities via multifaceted mechanisms that remain incompletely understood (16).

This study examines the relationship between the sialic acid effect, cancer chemotherapy, and expression of the GD-2 antigen, emphasizing the significance of targeting sialylation in order to improve the sensitivity of cancer therapy, including chemotherapy. It also investigates the possibility of combining anti-GD-2 immunotherapy with temozolomide chemotherapy.

However, as exogenous sialic acid may not completely mimic endogenous hypersialylation, the current results should be considered mechanistic and hypothesis-generating. Overall, this study aimed to elucidate the role of changes in sialylation in astrocytoma therapy resistance and the ability of astrocytoma cells to undergo GD-2 targeted immunotherapy through the combined regulation of the inhibitory concentration of temozolomide and GD-2 synthase expression.

2. Methods

2.1 Chemicals

The sialic acid (NANA /Neu5Ac or N-acetylneuraminic) product and all other reagents were obtained from Sigma-Aldrich (St. Louis, MO, USA), Merck (Darmstadt, Germany), and Yekta Tajhiz Azma (Iran). Sialic Acid and Temozolomide solution stocks were prepared in sterile phosphate-buffered saline and sterilized through a 0.22 µm filter.

2.2 Cell culture (1321N1 astrocytoma cells)

The human astrocytoma cell line 1321N1 (NCBI C118) was provided by the IPI. The cells were cultured in Dulbecco's modified Eagle medium (DMEM; low glucose; Gibco), then supplemented with 10% heat-inactivated Fetal Bovine Serum (FBS; Gibco), and 1% penicillin-streptomycin antibiotic. These cultures were grown at room temperature under humidified conditions of 95% with 5% CO_2.

2.3 (MTT assay; $EC5_0/IC5_0$) for Cell viability and dose–response determination

According to prior findings, we explored the effects of sialic acid on cell toxicity. The 1321N1 cells were incubated with different concentrations of Sialic acid for approximately 24 hours, then their cytotoxic potential were evaluated using the MTT assays. Briefly, cell viability was assessed in sialic acid/TMZ/ and SA+TMZ treatment through the MTT assays. The EC50 of sialic acid involved the following experimental procedure: 1321N1 cells were seeded at 5×10^3 cells/well in 96-well plates and incubated for approximately 24 hours. The cells were then exposed to and Temozolomide at the specified final concentrations of 20, 50, 100, 300, 500, 700, 1000, 1100, 1200, 1300, 1400, and 2500 µM for Neu5Ac, and 10, 50, 100, 200, 400, 800, 1000, 1200, 1500, 1800 µM for Temozolomide for 24 hours. Then, a solution of 30 µL MTT (0.5 mg/mL in PBS) was added to the wells, and incubation was carried out at room temperature for approximately 4 hours. Formazan crystals were solubilized by adding 120 µL of DMSO, followed by shaking for 20 minutes. Absorbance value was recorded at 570 nm using a microplate reader (Bio Intellectica Scientific Inc., Canada). Each experimental condition was performed using three independent biological replicates, with four technical wells per biological replicate.

2.4 Gene expression analysis qRT-PCR for *GD-2 synthase*

Total RNA was extracted from cells treated with Neu5Ac/ TMZ/ SA+TMZ for 24 h using QIAzol reagent, according to the manufacturer's guidelines and protocols. The quality of the isolated RNA and its concentration were evaluated by agarose gel

This open-access article distributed under the terms of the Creative Commons Attribution- Noncommercial 4.0 International License

electrophoresis and NanoDrop, respectively. Genomic DNA contamination was eliminated using DNase I. Subsequently, a commercial cDNA synthesis kit, prepared by Yekta Tajhiz Azma Company was used in order to convert total RNA to cDNA. RT-qPCR was carried out in a total volume of 10 µL. Reactions were conducted using 2 µL of cDNA template, 5 µL of SYBR Green Master Mix, and 0.8 µL (5 µM) of each primer (Table 1). The programme used for amplification included an initial step at 94 °C for 3min, followed by 40 cycles at 94 °C for 10 s, and extension at 60 °C for 30 s. An internal reference gene was used after confirming its expression stability under the experimental treatments. Relative expression was calculated using the 2 –ΔΔCt Formula. RT-qPCR assays were performed using three biological replicates while each was run in technical duplicate.

Table 1. Primer Sequences for the target gene

gene ID	name	strand	Primer 5' →3'	Product size	Annealing Tm
2583 NC_000012	*B4GALNT1 (GD-2 synthase)*	-	F: CAA CTC CCC GCT CCA GTA CC	98 bp	62.24
			R: CCT GAC CAG AAG CTG CCT GAA		62.33
60 NC_000007	*ACTB*	-	F: GAG CAT CCC CCA AAG TTC ACA	103 bp	60.55
			R: GGG ACT TCC TGT AAC AAC GCA		60.54

3. Results

3.1. 1321N1 cell viability

Treatment of 1321N1 cells with Sialic Acid resulted in a concentration-dependent change in metabolic activity as measured by MTT. The Cell populations were categorized into four groups: a control group (untreated 1321N1 cells) and three treatment groups exposed to Sialic Acid (concentration range: 0.02–2500 µM), TMZ (concentration range: 10-1800 µM) for 24 h. The $EC5_0$ = 490.1 µM and $IC5_0$ = 1296 µM were reported in our previous study (Figure 1A–B). The IC50 for TMZ/ and TMZ + SA (EC) were 441.6 µM and 1109 µM, respectively. Data are presented as the mean ± standard deviation (SD), and differences were considered statistically significant at $p < 0.05$.

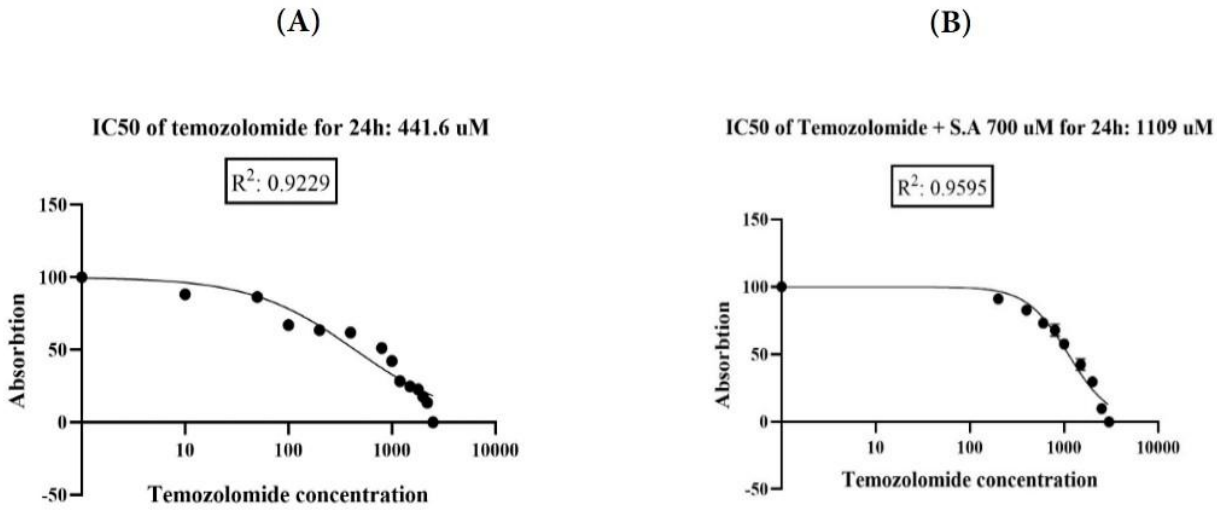


Figure 1. IC50 assessment of Temozolomide and IC50 changing assessment of Temozolomide in combination with Sialic acid. (A) Concentration–response curve showing the inhibitory concentration (IC50 = 441.6 µM) of TMZ that reduces 1321N1 cell viability after 24 h. (B) Concentration–response curve showing the inhibitory concentration (IC50 = 1109 µM) of TMZ in the presence of an enhanced concentration of sialic acid after 24 h. The method used to represent data is the mean ± SD, (p-value < 0.05).

3.2 Relative expression level of GALNT1 in 1321N1 Cell line.

After the sialic acid treatment, GD2 synthase expression level decreased significantly to 0.174 ± 0.1 (p-value=0.002), In contrast, the TMZ treatment did not significantly change the expression level of GD2 synthase (1.001 ± 0.004, p-value=0.43). On the other hand, Combined treatment with SA and TMZ resulted in reduction of expression of GD2 synthase to 0.38 ± 0.11 (p-v value=0.04) (Figure 2). Thus, we can

This open-access article distributed under the terms of the Creative Commons Attribution- Noncommercial 4.0 International License

conclude that TMZ can slightly attenuate the inhibitory effect of sialic acid.

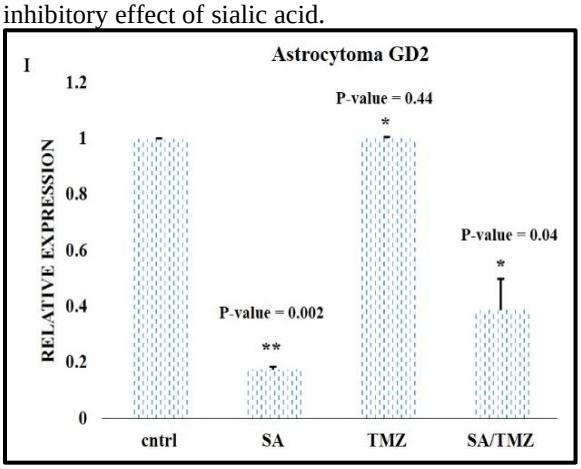


Figure 2. GD2 synthase under conditions of sialic acid/Temozolomide/ sialic acid + Temozolomide

General findings include i) modification of the cytotoxic effect of TMZ, ii) GD-2 synthase gene expression in astrocytoma cells, iii) non-significant and very slight induction of GD-2 synthase gene expression in the TMZ exposure experiment, and iv) reduction of the TMZ effect on GD-2 gene expression by sialic acid, as demonstrated in Fig. 2.

4. Discussion

We examined the effects of sialic acid administered alone or combined with temozolomide, aimed at enhancing GD2 expression level. First, the negative influence of sialic acid on the cytotoxic properties of TMZ was observed. Second, it was demonstrated that treatment with temozolomide alone did not significantly change the expression level of B4GALNT1. Thus, we can conclude that chemotherapy with TMZ may not interfere with GD-2 immunotherapy.

One of the hallmarks of cancer cells is hypersialylation, which may contribute to metastasis formation (17-19), chemoresistance (20, 21), and stromal–mediated immunosuppression in the tumor Microenvironment (22). Numerous studies have confirmed the possibility of using abnormal sialylation as an innovative approach in the treatment of drug resistance. In agreement with our previous findings and those of other scientific groups, we have found that sialylation plays a role in the acquisition of a metastatic phenotype through its effect on MMP9 (17), PDGFD, NRP-1, VEGF/ VEGFR, and ERK1/2 and p-ERK1/2 (18), as well as in chemotherapy resistance through ABCC1 upregulation (23). Furthermore, we previously reported the anti-inflammatory potential of sialic acid (24). In this study, we demonstrated that treatment with sialic acid can decrease the cytotoxicity of TMZ. TMZ can induce B4GALNT1 expression (GD2 synthase), which can be attenuated by the sialic acid inhibitory effect.

The B4GALNT1 gene encodes β-1,4-N-acetyl-galactosaminyltransferase1, a key glycosyltransferase involved in the biosynthesis of gangliosides. Specifically, it attaches GalNAc to GM3 and GD3 through a β-1,4 linkage, yielding GM2 and GD2, respectively. As such, B4GALNT1 is involved in carbohydrate and lipid metabolism metabolism, with a special function in the synthesis of glycosphingolipids (25). Research on breast cancer has shown that silencing B4GALNT1 and ST8SIA1 resulted in decreased expression of GD2 and GD3, causing a shift in phenotype from Cancer Stem Cells (CSC) to non-CSC cells, as detected by a reduction in mammospheres and cell motility (26).

The findings of our study are especially important since the particular role of sialic acid was demonstrated in the promotion of cancer cell proliferation, anti-inflammatory activity, and suppression of the immune system. However, the relationship between the intracellular concentration of sialic acid and disialoganglioside synthesis requires further investigation. It was revealed that GD-2 can serve as an antigen on the surface of the astrocytoma cell and It was revealed that GD-2 could serve as an antigen on the surface of the astrocytoma cell and that sialic acid may attenuate the otherwise non-significant positive effect of temozolomide on GD2 expression. Additional experiments are required to confirm these findings.

Both GD3 synthase and, particularly, GD2 synthase gene expressions are epigenetically controlled (27). Evidence has been provided by van den Bijgaart et al. (28), who examined the epigenetic modulation of the GD2 synthase gene in neuroblastoma cells with endogenous GD2 synthesis capacity, focusing on the effects of sialic acid supplementation with HDAC inhibition (28).

Our quantitative findings provide critical insight into the interplay between sialic acid and chemoresistance. The potential role of hypersialylation in inducing drug resistance was reflected in the shift in the dose-response profile, especially as the IC50 of TMZ increased from 441.5to 1109 following sialic acid treatment, indicating a profound reduction in drug sensitivity. This resistance mechanism is further corroborated by the marked reduction in GD2 synthase expression after sialic acid treatment (0.174 ± 0.1, p-value= 0.002), which underscores its role in modulating the immunogenic profile of astrocytoma cells. Although TMZ treatment alone showed no significant effect on GD2 synthase (1.001 ± 0.004, p-value = 0.44), the observed reduction in the

This open-access article distributed under the terms of the Creative Commons Attribution- Noncommercial 4.0 International License

combination group (0.38 ± 0.11, p-value = 0.04) suggests that TMZ provides only marginal mitigation of the sialic acid- induced downregulation. Collectively, these data imply that monotherapy with TMZ may be insufficient to overcome the antigen masking caused by hypersialylation and the sialic acid pathway simultaneously.

While our findings from in vitro models provide compelling evidence for the role of hypersialylation in chemoresistance, we acknowledge the inherent limitations of cell culture systems in replicating the complexity of the tumor microenvironment. Therefore, further validation of these mechanisms in in vivo models is essential to confirm the translational potential of these findings for clinical applications.
Building upon these considerations, further research needs to be conducted in order to investigate whether the inhibition of HDACs could control the stability of the expression of GD2 synthase and sialyltransferase. Furthermore, it is important to analyze the expression levels of other glycosphingolipids that are synthesized through the reaction of GD2 synthase and sialyltransferase, as well as GD2 itself (for example, GD1b). Analysis by means of mass spectrometry would be very helpful in this regard (28).
Consistent with previous research on neuroblastoma cells, which has highlighted immunotherapeutic strategies such as monoclonal antibodies, the expression of the GD2 antigen on the surface is recognized as a critical target for carbohydrate vaccines and CAR -T cell therapies. However, existing studies indicate that the co-administration of sialic acid and HDACi promotes GD2 upregulation in neuroblastoma cells, thereby improving the impact of GD2-targeted immunotherapy in diagnosed patients. (28). In contrast, we argue that sialic acid supplementation can induce drug resistance and that targeting sialylation abnormalities combined with chemotherapy may increase the efficiency of GD2-targeted immunotherapy in patients with astrocytoma.

5. Conclusions

Our findings indicate that sialic acid may reduce the efficacy and functional activity of anticancer agents, potentially resulting in treatment failure. Hence, the target of treatment in such cases needs to be the sialylation process. Thus, a combination treatment may be needed for the treatment of glioma cancer. This paper provides a theoretical and practical background for understanding the impact of sialic acid on the 1321N1 cell line, which can help identify strategies to combat glioma progression.

Acknowledgements

The authors express gratitude to Tahere Seifi for valuable contributions to the present study.

Ethical Considerations and Compliance with Ethical Guidelines

This study was conducted in accordance with the ethical standards of the Faculty of Cellular and Molecular Biology, Islamic Azad University, Tehran, Iran, and approved with the code of ethics IR.IAU.PS.REC.1401.435.

Funding

The authors declare that no funding, grants, or financial support from any university, institution, or individual was received for the conduct of this research.

Conflict of interest

The authors reported no conflicts of interest in this work.

Author contributions

HH, HG, and MH designed the research. HH, and HG performed and analyzed real-time PCR. HH cultured GB cells and treated them with sialic acid, Temozolomide, SA +TMZ. HH, HG and MH performed statistical analyses. Conceptualization: HH, HG, and MH; Data curation: AS and MH; Methodology: HH and HG; Writing the original draft: HH; Writing, review, and editing: HG and MH, who provided important research advice and revised the manuscript. All co-authors read and accepted the manuscript.

AI Using Declaration

ChatGPT was used for language and grammar corrections. The final output was read and modified by all authors.

6. References

1. Silverstein MD, Cascino TL, Harmsen WS. High-grade astrocytomas: resource use, clinical outcomes and cost of care. Mayo Clin Proc. 1996(10):936-44. (DOI: 10.1016/S0025-6196(11)63766-X) (PMID)
2. Jaeckle KA, Decker PA, Ballman KV, Flynn PJ, Giannini C, Scheithauer BW, et al. Transformation of low-grade glioma and correlation with outcome: an NCCTG database analysis. J Neurooncol. 2011;104(1):253-9. (DOI: 10.1007/s11060-010-0476-2) (PMID)
3. Rotta JM, de Oliveira MF, Reis RC, Botelho RV. Malignant transformation of low-grade gliomas in patients undergoing adjuvant therapy. Acta Neurol Belg. 2017;117(1):235-9. (DOI: 10.1007/s13760-016-0657-7) (PMID)

This open-access article distributed under the terms of the Creative Commons Attribution- Noncommercial 4.0 International License

4. Yalamarty SSK, Filipczak N, Li X, Subhan MA, Parveen F, Ataide JA, Torchilin VP. Mechanisms of resistance and current treatment options for glioblastoma multiforme (GBM). Cancers. 2023;15(7):2116. (DOI: 10.3390/cancers15072116) (PMID)
5. Yuzhalin AE. New experimental therapies for glioblastoma: a review of preclinical research. Acta Neuropathol Commun. 2025:13(1):199. (DOI: 10.1186/s40478-025-02105-w) (PMID)
6. Rotta JM, de Oliveira MF, Reis RC, Botelho RV. Malignant transformation of low-grade gliomas in patients undergoing adjuvant therapy. Acta Neurol Belg. 2017;117(1):235-9. (DOI: 10.1007/s13760-016-0657-7) (PMID)
7. Van den Bent MJ, Taphoorn MJB, Brandes AA, Menten J, Stupp R, Frenay M, et al. Phase II study of first-line chemotherapy with temozolomide in recurrent oligodendroglial tumors: the European Organization for research and treatment of Cancer Brain Tumor Group study 26971. J Clin Oncol. 2003;21(13):2525-8. (DOI: 10.1200/JCO.2003.12.015) (PMID)
8. Jezierzański M, Nafalska N, Stopyra M, Furgoł T, Miciak M, Kabut J, et al. Temozolomide (TMZ) in the treatment of glioblastoma multiforme—a literature review and clinical outcomes. Curr Oncol. 2024;31(7):3994-4002. (DOI: 10.3390/curroncol31070296) (PMID)
9. Pace A, Vidiri A, Galie E, Carosi M, Telera S, Cianciulli AM, et al. Temozolomide chemotherapy for progressive low-grade glioma: clinical benefits and radiological response. Ann Oncol. 2003:14(12):1722-6. (DOI: 10.1093/annonc/mdg502) (PMID)
10. Yasinjan F, Xing Y, Geng H, Guo R, Yang L, Liu Z, et al. Immunotherapy: a promising approach for glioma treatment. Front Immunol. 2023;14:1255611. (DOI: 10.3389/fimmu.2023.1255611) (PMID)
11. Gong G, Jiang L, Zhou J, Su Y. Advancements in targeted and immunotherapy strategies for glioma: toward precision treatment. Front Immunol. 2025;15:1537013. (DOI: 10.3389/fimmu.2024.1537013) (PMID)
12. Sait S, Modak S. Anti-GD2 immunotherapy for neuroblastoma. Expert Rev Anticancer Ther. 2017;17(10):889-904. (DOI: 10.1080/14737140.2017.1364995) (PMID)
13. Philippova J, Shevchenko J, Sennikov S. Gd2-targeting therapy: a comparative analysis of approaches and promising directions. Front Immunol. 2024;15:1371345. (DOI: 10.3389/fimmu.2024.1371345) (PMID)
14. Mora J, Chan GC, Morgenstern DA, Amoroso L, Nysom K, Faber J, et al. The anti-GD2 monoclonal antibody naxitamab plus gm-gsf for relapsed or refractory high-risk neuroblastoma: a phase 2 clinical trial. Nature Commun. 2025;16(1):1636. (DOI: 10.1038/s41467-025-56619-x) (PMID)
15. Marx S, Wilken F, Wagner I, Marx M, Troschke-Meurer S, Zumpe M, et al. Gd2 targeting by dinutuximab beta is a promising immunotherapeutic approach against malignant glioma. J Neurooncol. 2020;147(3):577-85. (DOI: 10.1007/s11060-020-03470-3) (PMID)
16. Farrell RE, Stelzer KA, Liu GJ, Skropeta D. Emerging role of sialylation in cancer therapy resistance: mechanisms and therapeutic implications. Drug Resist Update. 2025;101285. (DOI: 10.1016/j.drup.2025.101285) (PMID)
17. Shabani Sadr NK, Shafiei M, Galehdari H, Khirolah A. The effect of sialic acid on the expression of miR-218, NF-κB, MMP-9, and timp-1. Biochemical Genetics. 2020;58(6):883-900. (DOI: 10.1007/s10528-020-09981-y) (PMID)
18. Seifi T, Shafiei M, Rahimi K, Ghaedi K, Galehdari H. Up-regulation of PDGF-D and nrp-1 in the Glioma cell line 1321n1 attributed to sialic acid treatment: mini-review and findings. Jentashapir, J Cell Mol Biol. 2022;13(2). (DOI: 10.5812/jjcmb-130150)
19. Dobie C, Skropeta D. Insights into the role of sialylation in cancer progression and metastasis. Br J Cancer. 2021;124(1):76-90. (DOI: 10.1038/s41416-020-01126-7) (PMID)
20. Zhu J, Wang A, Tong H, Sun Y, Li T, Wu L, et al. Abnormal sialylation promotes chemotherapy resistance in bladder cancer via the pi3k-akt-mtor signaling pathway. Cancers. 2026;18(11):1713. (DOI: 10.3390/cancers18111713) (PMID)
21. Farrell RE, Stelzer KA, Liu GJ, Skropeta D. Emerging role of sialylation in cancer therapy resistance: mechanisms and therapeutic implications. Drug Resist Update. 2025;101285. (DOI: 10.1016/j.drup.2025.101285) (PMID)
22. O'Neill A, Zakaria N, Egan H, Treacy O, Hogan AM, O'Dwyer M, et al. The tumour glyco-code: sialylation as a mediator of stromal cell immunosuppression in the tumour microenvironment. Eur J Immunol. 2025;55(7),e70000. (DOI: 10.1002/eji.70000) (PMID)
23. Rezaei F, Shafiei M, Galehdari H, Malayeri A, Kalantar SM. Exploring the influence of sialic acid on drug resistance in glioma: a focus on ABCB1 and abcc1 transporter gene expression. Jentashapir J Cell Mol Biol. 2024;15(1):e142488. (DOI: 10.5812/jjcmb-142488)
24. Payazdan M, Khatami S, Galehdari H, Delfan N, Shafiei M, Heydaran S. The anti-inflammatory effects of sialic acid on human glial cells by the upregulation of IL-4 and IL-10 gene expression. Gene Rep. 2021;24:101218. (DOI: 10.1016/j.genrep.2021.101218)
25. Yamaguchi T, Yamauchi Y, Furukawa K, Ohmi Y, Ohkawa Y, Zhang Q, et al. Expression of b4galnt1, an essential glycosyltransferase for the synthesis of complex gangliosides, suppresses bace1 degradation and modulates app processing. Sci Rep. 2016;6(1):34505. (DOI: 10.1038/srep34505) (PMID)
26. O'Neill NS, Rizk M, Li AX, Martin TA, Jiang WG, Mokbel K. Correlation of gd2 biosynthesis enzymes with cancer stem cell markers in human breast cancer. Cancer Genomics Proteomics. 2025;22(2):231-46. (DOI: 10.21873/cgp.20498) (PMID)
27. Suzuki Y, Yanagisawa M, Ariga T, Yu RK. Histone acetylation-mediated glycosyltransferase gene regulation in mouse brain during development. J Neurochem. 2011;116(5):874-80. (DOI: 10.1111/j.1471-4159.2010.07042.x) (PMID)

This open-access article distributed under the terms of the Creative Commons Attribution- Noncommercial 4.0 International License

Archives of Advances in Biosciences

28. van den Bijgaart RJ, Kroesen M, Wassink M, Brok I C, Kers-Rebel E D, Boon L, et al. Combined sialic acid and histone deacetylase (HDAC) inhibitor treatment up-regulates the neuroblastoma antigen GD2. J Biol Chem. 2019;294(12):4437-49. (DOI: 10.1074/jbc.RA118.002763) (PMID)

This open-access article distributed under the terms of the Creative Commons Attribution- Noncommercial 4.0 International License