Proceedings of the 6th International Conference on Biological Engineering and Medical Science
DOI: 10.54254/2753-8818/2026.38114

AI Integration of Multi-omics Data for Drug Target Prediction in Glioblastoma

Yuchen Gao

Department of Pharmacology and Therapeutics, University of Liverpool, Liverpool, UK
g1907664579@outlook.com

Abstract. Glioblastoma (GBM) is an aggressive primary brain tumor with marked molecular and cellular heterogeneity, and current treatment provides limited long-term disease control. Single-target therapies have frequently failed because tumor subpopulations can differ in signaling dependencies, adapt under treatment pressure, and interact with a complex microenvironment. This review examines how artificial intelligence (AI) can integrate multi-omics data to improve drug-target prediction in GBM. It summarizes the pathological and molecular basis of GBM, evaluates current therapeutic targets and their limitations, and compares genomic, transcriptomic, single-cell, spatial, proteomic, metabolomic, and imaging data used for target discovery. Machine-learning, deep-learning, and network-based approaches are discussed with examples of multimodal risk stratification and candidate-target identification. The review also evaluates CRISPR screening as a functional validation step that can distinguish statistical associations from genuine tumor dependencies. Overall, AI-integrated multi-omics can provide a more context-specific approach to target prioritization by linking candidate genes to patient subgroups, cell states, and pathway activity. However, small cohorts, missing data, batch effects, limited model generalizability, and insufficient experimental validation remain major barriers. Future studies should combine larger multi-centre datasets with longitudinal and spatial profiling, interpretable models, functional perturbation, and prospective validation to support clinically translatable precision therapy in GBM.

Keywords: Glioblastoma, multi-omics, artificial intelligence, drug target prediction, CRISPR screening

1. Introduction

Glioblastoma (GBM) is the most common and lethal primary malignant brain tumor in adults; despite maximal safe resection combined with radiotherapy and temozolomide chemotherapy, median overall survival remains approximately 12–15 months [1]. The World Health Organization's 2021 classification of central nervous system tumors emphasizes that GBM is defined not only by histological grade but by a specific constellation of molecular alterations, including isocitrate dehydrogenase (IDH)-wildtype status, epidermal growth factor receptor (EGFR) amplification, telomerase reverse transcriptase (TERT) promoter mutation, and chromosome 7 gain/chromosome 10 loss [2]. A central obstacle to effective treatment is the tumor's extraordinary inter- and intra-

© 2026 The Authors. This is an open access article distributed under the terms of the Creative Commons Attribution License 4.0 (https://creativecommons.org/licenses/by/4.0/).

DOI: 10.54254/2753-8818/2026.38114

tumoral heterogeneity. Bulk genomic profiling by the Cancer Genome Atlas first defined proneural, neural, classical, and mesenchymal transcriptional subtypes of GBM [3], and subsequent single-cell RNA sequencing has shown that individual tumors in fact harbor a continuum of malignant cell states that coexist within a single lesion and can shift under therapeutic pressure [4-6]. This heterogeneity, together with an immunosuppressive, highly vascularized microenvironment, has repeatedly undermined single-target therapies such as receptor tyrosine kinase inhibitors directed at EGFR, which have shown limited clinical benefit despite strong pre-clinical rationale [7].

These challenges have resulted in recent research focusing on the integration of multiple omic layers (genomics, transcriptomics, single-cell and spatial profiles, and proteomics) with artificial intelligence (AI) and machine-learning algorithms for systematic identification and prioritization of drug targets as opposed to single-modality or pathway-driven approaches. Spatially resolved multi-omics analyzes have mapped out bidirectional signaling between tumor and stroma/immune compartments, revealing region-specific vulnerabilities that bulk sequencing obscures [8]. More recently, machine learning frameworks trained on multi-omics datasets – integrating radiomic, genomic, transcriptomic and proteomic features across large patient cohorts – have been employed for risk stratification and nominated candidate therapeutic targets associated with high-risk molecular subgroups of GBM [9]. In total, these studies represent a general methodological shift from single data types or expert-curated pathway knowledge toward AI-based models that can learn cross-omics patterns more representative of the biological complexity of GBM and provide a data-driven complement to traditional hypothesis-driven target discovery [10].

However, there is no consensus framework yet on how to best integrate heterogeneous multi-omics data with AI to prioritize druggable, clinically translatable targets in GBM. Many computationally nominated candidates still need experimental and clinical validation. Addressing this gap has both scientific and clinical implications. A validated AI-multi-omics pipeline could accelerate target discovery timelines, reduce dependence on single pathway assumptions, and aid in pairing patients with therapies tailored to the unique molecular and cellular makeup of their tumor — advancing more precise, personalized treatment strategies for a disease that has historically had poor outcomes. More generally, this review seeks to offer a systematic reference point for future computational and experimental work by laying out the data modalities and computational approaches that have proved most informative for GBM target discovery up to now. This mapping will help future researchers avoid the replication of existing pipelines and will also highlight where the most critical methodological gaps remain.

Therefore, the pathological pathways and molecular heterogeneity of GBM are reviewed, current and AI/multi-omics-nominated therapeutic targets are examined, including the data modalities and machine-learning techniques used to identify them, and the strengths, limitations, and translational challenges of AI-driven multi-omics target prediction are considered, before a summary of key findings and future directions is presented.

2. GBM: disease background and therapeutic targets

2.1. Pathological mechanisms and molecular classification

GBM is classified by the World Health Organization (WHO) as a grade 4 diffuse astrocytic tumor. Histologically, it shows marked nuclear atypia, high mitotic activity, microvascular proliferation, and pseudo palisading necrosis, all of which are consistent with rapid growth and invasion [2]. The 2021 WHO classification places greater emphasis on molecular features. An adult-type diffuse glioma can be classified as GBM when it is isocitrate dehydrogenase (IDH)-wildtype and contains at

DOI: 10.54254/2753-8818/2026.38114

least one of the following alterations: epidermal growth factor receptor (EGFR) amplification, telomerase reverse transcriptase (TERT) promoter mutation, or combined whole-chromosome 7 gain and chromosome 10 loss. This classification can apply even when classic grade 4 histological features are not present [2]. These criteria also separate IDH-wildtype GBM from IDH-mutant astrocytoma, which follows a different biological and clinical course.

Several additional molecular changes contribute to GBM progression. Three signaling systems are frequently disrupted. The first is the receptor tyrosine kinase (RTK)/RAS/phosphoinositide 3-kinase (PI3K) pathway, often affected by EGFR amplification or phosphatase and tensin homolog (PTEN) loss. The second is the tumor protein p53 (TP53) pathway, which can be altered through TP53 mutation or mouse double minute 2/4 (MDM2/MDM4) amplification. The third is the retinoblastoma (RB) pathway, where cyclin-dependent kinase inhibitor 2A/B (CDKN2A/B) deletion or cyclin-dependent kinase 4 (CDK4) amplification is common [1, 2]. Bulk transcriptomic analysis by The Cancer Genome Atlas identified proneural, neural, classical, and mesenchymal transcriptional subtypes [3]. But a bulk sample is an average of many different cells. Single-cell RNA sequencing showed a more complex picture, with several malignant cell states coexisting in the same tumor [4]. Neftel et al. described four major states: neural-progenitor-like, oligodendrocyte-progenitor-like, astrocyte-like, and mesenchymal-like states [5]. The balance between these states is affected by genetic changes and local environmental conditions. For example, CDK4 amplification is associated with progenitor-like programs, whereas neurofibromin 1 (NF1) loss is associated with the mesenchymal state [5]. Hypoxia and treatment can also alter the composition of cell states. This plasticity may explain why a therapy can eradicate one population, yet allow another to persist and grow [5, 6]. Together with the immunosuppressive and highly vascularized tumor microenvironment, these results support the notion of GBM as a dynamic tumor ecosystem rather than a uniform disease.

2.2. Current therapeutic targets and their limitations

The standard treatment for newly diagnosed GBM consists of maximal safe surgical resection followed by radiotherapy with concurrent temozolomide (TMZ), and then adjuvant TMZ. This approach has remained the main treatment backbone for approximately two decades, but median overall survival is still around 12–15 months [1]. O6-methylguanine-DNA methyltransferase (MGMT) promoter methylation is one of the most clinically useful biomarkers. Reduced MGMT expression limits repair of TMZ-induced DNA damage, so MGMT-methylated tumors generally respond better to TMZ. However, MGMT status is mainly a predictive and prognostic biomarker rather than a drug target itself [1, 2]. The limited improvement achieved by additional targeted agents shows that new targets must be selected in a way that accounts for molecular heterogeneity and treatment resistance.

Several molecular and microenvironmental targets have been tested in GBM, but clinical benefit has often been limited. EGFR is amplified or mutated in many tumors, and the constitutively active epidermal growth factor receptor variant III (EGFRvIII) has been a prominent target. Small-molecule EGFR inhibitors such as erlotinib and gefitinib have not produced consistent benefit in unselected GBM populations [7]. EGFRvIII-directed approaches have faced a related problem: the antigen is not expressed by every tumor cell and can be lost during treatment. Anti-angiogenic therapy provides another example. Bevacizumab, an antibody against vascular endothelial growth factor A (VEGF-A), can delay progression and reduce edema, but randomized studies have not demonstrated a clear overall-survival advantage when it is added to standard treatment or combined with lomustine at recurrence [11, 12]. Immune checkpoint inhibition has also been disappointing. In

DOI: 10.54254/2753-8818/2026.38114

the CheckMate 143 trial, the programmed cell death protein 1 (PD-1) antibody nivolumab did not improve overall survival compared with bevacizumab in recurrent GBM [13]. These outcomes reflect several barriers, including blood–brain barrier penetration, compensatory signaling, a myeloid-dominated immunosuppressive microenvironment, limited T-cell infiltration, and substantial intratumoral heterogeneity. They also show why selecting one highly expressed molecule is not sufficient. A more useful target-discovery strategy should combine molecular abundance with cell-state specificity, pathway context, functional dependency, and evidence that the target is druggable.

3. AI-integrated multi-omics approaches for target prediction in GBM

3.1. Multi-omics data modalities relevant to target discovery

AI-driven target discovery in GBM uses complementary data types that describe different levels of tumor biology. Genomic data identify mutations, copy-number changes, and structural alterations, while bulk transcriptomic data measure gene-expression programs across the whole sample. Single-cell RNA sequencing (scRNA-seq) adds cell-level resolution and can identify malignant states or rare treatment-resistant populations that are hidden in bulk measurements [4-6]. Spatial methods preserve tissue location and can connect molecular programs with local microenvironmental conditions. Ravi et al. combined spatial transcriptomics, metabolomics, proteomics, metabolic imaging, imaging mass cytometry, and inferred copy-number alterations in GBM [8]. Their analysis showed spatial segregation of lineage states and region-specific adaptation to inflammatory and metabolic stress. It also linked tumor subclones with local reactive transcriptional programs, supporting the idea that environmental pressure can reshape malignant cell states [8]. This is important for target discovery because a dependency found in a hypoxic or inflammatory region may not be detectable when signals from the whole tumor are average.

Proteomic and phosphoproteomic data provide information that is closer to drug action because most drugs act on proteins rather than RNA. These data can reveal protein abundance, phosphorylation, and active signaling pathways that are not reliably predicted from mRNA levels alone. Metabolomic measurements can further describe nutrient use and stress adaptation. Radiomic features derived from magnetic resonance imaging (MRI) provide a non-invasive view of tumor phenotype and can be collected longitudinally [9]. Functional screening should be considered separately from the omics layers. Clustered regularly interspaced short palindromic repeats (CRISPR)-based knockout or interference screens do not simply describe a molecular state; they test whether loss of a gene changes cell fitness or treatment response. For this reason, CRISPR is particularly useful as a validation step after computational target nomination. MacLeod et al., for example, screened 30 patient-derived GBM stem-cell cultures and identified both conserved and state-specific dependencies. Developmental-state cells and injury-response-state cells showed different vulnerabilities, including distinct cyclin D dependencies and sensitivity to integrin, focal adhesion kinase, mitogen-activated protein kinase kinase (MEK), and OLIG2 pathway inhibition [14, 15]. Such functional evidence can help distinguish a correlated biomarker from a target that the tumor actually depends on.

3.2. Machine learning and AI methods for target prioritization

Machine-learning methods can be selected according to the structure of the available data and the prediction task. Classical supervised models include random forests, support vector machines, and

DOI: 10.54254/2753-8818/2026.38114

gradient-boosted trees such as extreme gradient boosting (XGBoost). These approaches work well with tabular features such as gene expression, mutation status, copy-number values, protein abundance, and radiomic measurements. Feature-importance methods can then identify which variables contribute most strongly to a prediction. Feature-importance scores can help rank variables associated with a model prediction, but they should not be interpreted as evidence of causal dependency. Zhang et al. integrated radiomic, pathomic, genomic, transcriptomic, and proteomic data from patients with IDH-wildtype GBM [9]. A complete five-modality dataset was available for 147 patients. Their machine-learning analysis separated patients into two clinically different risk groups. The high-risk group showed stronger proliferation and cell-cycle activity, and downstream analysis nominated protein disulfide isomerase family A member 4 (PDIA4), eukaryotic translation initiation factor 3 subunit I (EIF3I), and RFT1 homolog (RFT1) as potential biomarkers and therapeutic targets [9]. This example shows how multimodal prediction can move from patient stratification to a shorter list of biologically relevant candidates.

Deep-learning methods are useful when the number of features is very large or when several data modalities must be combined [16, 17]. Autoencoders can compress high-dimensional omics data into a smaller latent representation, which can then support clustering, classification, survival prediction, or subtype discovery. A glioma-specific example is DeepAutoGlioma, which integrated transcriptomic and methylation data using an autoencoder and then applied artificial neural networks and convolutional neural networks (CNNs) for glioma subtype classification [18]. By contrast, the framework reported by Zhang et al. is better described as a multimodal machine-learning approach: it combined imaging-derived radiomics and pathomics with genomic, transcriptomic, and proteomic information to generate risk groups and nominate candidate molecular targets [9]. Deep learning and other multimodal AI approaches can reveal relationships across data types that would be difficult to model manually, but their outputs still require biological interpretation and experimental validation [17].

Graph-based approaches add another level of biological context. In a graph neural network (GNN), genes or proteins can be represented as nodes and known protein–protein interactions or regulatory relationships as edges. Expression, mutation, protein abundance, or other measurements can then be attached to each node. This design allows the model to consider whether a candidate is important because of its position in a disease network rather than because of one unusually high measurement. Multimodal systems can also use separate model branches for different data types and merge their outputs through concatenation or attention mechanisms. Regardless of model type, the workflow should include data quality control, normalization, batch-effect correction, feature selection or dimensionality reduction, training with cross-validation, and testing in an independent dataset where possible [15, 17]. Model output should then be connected to functional evidence. CRISPR screens, perturbation experiments, drug-sensitivity datasets, and patient-derived models can test whether a predicted gene is necessary for tumor growth or treatment resistance. This step is essential because a strong statistical association does not by itself demonstrate that inhibiting the gene will produce a therapeutic effect.

3.3. From computational prediction to therapeutic target validation

A useful AI–multi-omics pipeline should narrow a large molecular search space into candidates that satisfy several conditions: association with aggressive disease, evidence of activity in relevant tumor cells, functional dependence, druggability, and preferably selectivity over normal brain tissue. A study by Zhang et al. illustrates the first part of this process. Their integrated model linked a high-risk GBM subgroup to proliferative and cell-cycle programs and highlighted PDIA4, EIF3I, and

DOI: 10.54254/2753-8818/2026.38114

RFT1 [9]. These candidates are more informative than genes selected from differential expression alone because they were identified in the context of multiple molecular and imaging layers. Nevertheless, computational nomination is still an early step. A target can be strongly associated with poor prognosis without being required for tumor survival, and a genetically essential target may still be unsuitable if it cannot be inhibited safely or if the drug does not reach the brain.

Functional genomics can strengthen this validation process. MacLeod et al. used CRISPR fitness screening across 30 patient-derived GBM stem-cell cultures and found that genetic dependencies varied along developmental and injury-response cell states [14]. This result is especially relevant to GBM because it suggests that a target may be effective only in a defined cellular context. Wang et al. used genome-wide CRISPR screens in both chimeric antigen receptor (CAR) T cells and patient-derived GBM stem cells [16]. The screens identified TLE4 and IKZF2 as regulators of CAR T-cell effector function and RELA and NPLOC4 as tumor-cell genes affecting susceptibility to CAR-mediated killing [16]. These experiments demonstrate how computational or molecular observations can be converted into testable dependencies and combination strategies. They also show that target discovery does not need to focus exclusively on malignant-cell growth; targets that modify immune sensitivity may be equally important.

The strongest future pipelines are therefore likely to use multi-stage evidence rather than one model score. Multi-omics and AI can identify candidates and define the patient or cell-state context in which they are most relevant. Network analysis can determine whether a candidate occupies a central or compensatory pathway position. CRISPR or pharmacological perturbation can then test causality, while patient-derived organoids, GBM stem-cell cultures, and in vivo models can assess efficacy and toxicity. Finally, blood–brain barrier penetration and pharmacokinetic properties must be considered before clinical translation. This sequence reduces the risk of prioritizing targets that are statistically interesting but biologically weak or therapeutically inaccessible.

4. Strengths, limitations, and translational challenges

4.1. Advantages of AI-integrated multi-omics

One major advantage of AI-integrated multi-omics is that it is closer to the biological structure of GBM than the single-data approach. Genomic alterations can pinpoint potential drivers, while transcriptomic and single-cell data can pinpoint which cell populations are expressing relevant programs. Proteomic data can measure pathway activity, and spatial data can locate these programs in specific microenvironmental niches. AI offers a practical approach to combine these high-dimensional measurements and detect patterns that could be missed when analyzing each data set separately [10, 15]. This is particularly valuable in GBM, where a target may be important only in a subpopulation or under a particular environmental condition.

Another advantage is better patient stratification. Instead of looking for one GBM target for everyone, multimodal models are able to make molecularly distinct groups and identify vulnerabilities unique to each group. For example, Zhang et al. described risk groups with cell-cycle and proliferating features that could be associated with specific candidate targets [9]. This approach is more in line with precision medicine as the treatment choice can be made based on a combination of tumor state and predicted dependency. Moreover, explainable machine-learning methods are able to rank important features that contribute to a prediction, which helps generate biological hypotheses to be tested experimentally.

DOI: 10.54254/2753-8818/2026.38114

4.2. Data and model limitations

Several limitations currently restrict the reliability of these approaches. Multi-omics datasets often contain relatively small patient numbers compared with the number of measured features. Missing modalities are common because not every patient has matched genomic, transcriptomic, proteomic, imaging, and spatial data. Different laboratories also use different sample-processing methods and sequencing platforms, creating batch effects that can be mistaken for biological signals. GBM adds further difficulty because tissue is usually obtained at surgery and therefore represents one location and one time point, while the tumor continues to evolve during treatment. A model trained on primary resection samples may not represent the molecular state of recurrent disease.

Model-related limitations are equally important. Complex deep-learning systems can overfit small datasets and may perform poorly when applied to patients from another hospital or population. High predictive accuracy also does not guarantee mechanistic validity. A model can exploit correlated features that are useful for classification but are not causal drivers of disease. Interpretability methods such as SHAP can help explain which features influence a prediction, but they do not prove that those features are therapeutic dependencies. Reviews of AI-assisted GBM discovery have therefore emphasized the need for larger studies, standardized protocols, external validation, and reproducible reporting before routine clinical use [15].

4.3. Clinical translation and future research

Clinical translation requires target prediction to be connected with experimental pharmacology. Candidate genes should first be tested in models that preserve GBM heterogeneity, including multiple patient-derived cultures, organoids, and orthotopic models. Functional screens should be repeated across molecular states so that broadly conserved dependencies can be distinguished from subgroup-specific vulnerabilities. Drug development must also address central nervous system exposure. A target may be biologically compelling but clinically impractical when available inhibitors have poor blood–brain barrier penetration or unacceptable toxicity. For this reason, druggability and pharmacokinetic information should be included earlier in target-ranking systems rather than considered only after biological validation.

Future work should also use longitudinal and spatial data more extensively. Single-cell and spatial profiling can identify which tumor or microenvironmental populations are responsible for a predicted signal and can guide rational combination therapy. Federated or multi-centre learning could help increase sample size while avoiding the need to centralize sensitive patient data. Most importantly, AI models should be prospectively evaluated, with predictions leading to pre-specified experiments, and successful targets tested in biomarker-selected clinical studies. This would elevate AI from a tool for retrospective pattern recognition to a reproducible framework for target discovery with measurable translational value.

5. Conclusion

GBM is still difficult to treat because of variations in molecular alterations, malignant cell states and tumor microenvironment between patients and within the same tumor. The present review demonstrates that these features constrain the effectiveness of traditional single-target strategies and provide a strong rationale for the integration of multiple layers of biological information. Genomic, transcriptomic, single-cell, spatial, proteomic, metabolomic, and imaging data offer complementary views on GBM, which can be integrated using machine learning and deep learning approaches to

DOI: 10.54254/2753-8818/2026.38114

enable patient stratification and target prioritization. Recent multimodal studies have moved beyond prognosis by linking high-risk tumor states to specific candidate targets, and functional CRISPR screening provides an important route for testing whether predicted targets represent true dependencies. The main insight is that AI is most useful when it forms one stage of an evidence chain rather than acting as an independent target generator. A clinically relevant candidate should be supported by cross-omics evidence, linked to a defined cell state or patient subgroup, validated experimentally, and assessed for druggability and brain exposure. Important limitations remain, including small and incomplete multi-omics cohorts, batch effects, model overfitting, limited external validation, and the difficulty of representing tumor evolution with a single surgical sample. Future research should therefore prioritize larger multi-centre datasets, longitudinal and spatial sampling, interpretable models, and systematic functional validation. Prospective studies that connect model predictions with experiments and biomarker-selected clinical testing will be essential if AI-integrated multi-omics is to contribute meaningfully to precision treatment for GBM.

References

[1] Lan, Z., Li, X., & Zhang, X. (2024). Glioblastoma: An update in pathology, molecular mechanisms and biomarkers. *International Journal of Molecular Sciences, 25*(5), 3040. https://doi.org/10.3390/ijms25053040

[2] Louis, D. N., Perry, A., Wesseling, P., Brat, D. J., Cree, I. A., Figarella-Branger, D., Hawkins, C., Ng, H. K., Pfister, S. M., Reifenberger, G., Soffietti, R., von Deimling, A., & Ellison, D. W. (2021). The 2021 WHO classification of tumors of the central nervous system: A summary. *Neuro-Oncology, 23*(8), 1231–1251. https://doi.org/10.1093/neuonc/noab106

[3] Verhaak, R. G. W., Hoadley, K. A., Purdom, E., Wang, V., Qi, Y., Wilkerson, M. D., Miller, C. R., Ding, L., Golub, T., Mesirov, J. P., & Cancer Genome Atlas Research Network. (2010). Integrated genomic analysis identifies clinically relevant subtypes of glioblastoma characterized by abnormalities in PDGFRA, IDH1, EGFR, and NF1. *Cancer Cell, 17*(1), 98–110. https://doi.org/10.1016/j.ccr.2009.12.020

[4] Patel, A. P., Tirosh, I., Trombetta, J. J., Shalek, A. K., Gillespie, S. M., Wakimoto, H., Cahill, D. P., Nahed, B. V., Curry, W. T., Martuza, R. L., Louis, D. N., Rozenblatt-Rosen, O., Suvà, M. L., Regev, A., & Bernstein, B. E. (2014). Single-cell RNA-seq highlights intratumoral heterogeneity in primary glioblastoma. *Science, 344*(6190), 1396–1401. https://doi.org/10.1126/science.1254257

[5] Neftel, C., Laffy, J., Filbin, M. G., Hara, T., Shore, M. E., Rahme, G. J., Richman, A. R., Silverbush, D., Shaw, M. L., Hebert, C. M., et al. (2019). An integrative model of cellular states, plasticity, and genetics for glioblastoma. *Cell, 178*(4), 835–849.e21. https://doi.org/10.1016/j.cell.2019.06.024

[6] Hernández Martínez, A., Madurga, R., García-Romero, N., & Ayuso-Sacido, Á. (2022). Unravelling glioblastoma heterogeneity by means of single-cell RNA sequencing. *Cancer Letters, 527*, 66–79. https://doi.org/10.1016/j.canlet.2021.12.008

[7] Qin, A., Musket, A., Musich, P. R., Schweitzer, J. B., & Xie, Q. (2021). Receptor tyrosine kinases as druggable targets in glioblastoma: Do signaling pathways matter? *Neuro-Oncology Advances, 3*(1), vdab133. https://doi.org/10.1093/noajnl/vdab133

[8] Ravi, V. M., Will, P., Kueckelhaus, J., Sun, N., et al. (2022). Spatially resolved multi-omics deciphers bidirectional tumor-host interdependence in glioblastoma. *Cancer Cell, 40*(6), 639–655.e13. https://doi.org/10.1016/j.ccell.2022.05.009

[9] Zhang, Z., Wang, Z., Li, R., Pei, D., Liu, J., Qiu, Y., Liu, Z., Wang, M., Ma, Z., Duan, W., et al. (2025). Machine learning model on multi-omics data enables risk stratification and identifies molecular heterogeneity and therapeutic targets in glioblastoma. *Research Square* [Preprint]. https://doi.org/10.21203/rs.3.rs-7510857/v1

[10] Pouyan, A., Ghorbanlo, M., Eslami, M., Jahanshahi, M., Ziaei, E., Salami, A., Mokhtari, K., Shahpasand, K., Farahani, N., Meybodi, T. E., Entezari, M., Taheriazam, A., Hushmandi, K., & Hashemi, M. (2025). Glioblastoma multiforme: Insights into pathogenesis, key signaling pathways, and therapeutic strategies. *Molecular Cancer, 24*(1), 58. https://doi.org/10.1186/s12943-025-02267-0

[11] Gilbert, M. R., Dignam, J. J., Armstrong, T. S., Wefel, J. S., Blumenthal, D. T., Vogelbaum, M. A., Colman, H., Chakravarti, A., Pugh, S., Won, M., et al. (2014). A randomized trial of bevacizumab for newly diagnosed glioblastoma. *New England Journal of Medicine, 370*(8), 699–708. https://doi.org/10.1056/NEJMoa1308573

DOI: 10.54254/2753-8818/2026.38114

[12] Wick, W., Gorlia, T., Bendszus, M., Taphoorn, M., Sahm, F., Harting, I., Brandes, A. A., Taal, W., Domont, J., Idbaih, A., et al. (2017). Lomustine and bevacizumab in progressive glioblastoma. *New England Journal of Medicine, 377*(20), 1954–1963. https://doi.org/10.1056/NEJMoa1707358

[13] Reardon, D. A., Brandes, A. A., Omuro, A., Mulholland, P., Lim, M., Wick, A., et al. (2020). Effect of nivolumab vs bevacizumab in patients with recurrent glioblastoma: The CheckMate 143 phase 3 randomized clinical trial. *JAMA Oncology, 6*(7), 1003–1010. https://doi.org/10.1001/jamaoncol.2020.1024

[14] MacLeod, G., Molaei, F., Haider, S., Almeida, M. P., Lin, S., Kushida, M., Sureshkumar, H., Bhatti, J. K., Lu, J. Q., Schramek, D., et al. (2024). Fitness screens map state-specific glioblastoma stem cell vulnerabilities. *Cancer Research, 84*(23), 3967–3983. https://doi.org/10.1158/0008-5472.CAN-23-4024

[15] Conte, L., Caruso, G., Philip, A. K., Cucci, F., De Nunzio, G., Cascio, D., & Caffo, M. (2025). Artificial intelligence-assisted drug and biomarker discovery for glioblastoma: A scoping review of the literature. *Cancers, 17*(4), 571. https://doi.org/10.3390/cancers17040571

[16] Wang, D., Prager, B. C., Gimple, R. C., et al. (2021). CRISPR screening of CAR T cells and cancer stem cells reveals critical dependencies for cell-based therapies. *Cancer Discovery, 11*(5), 1192–1211. https://doi.org/10.1158/2159-8290.CD-20-1243

[17] Lipkova, J., Chen, R. J., Chen, B., Lu, M. Y., Barbieri, M., Shao, D., Vaidya, A. J., Chen, C., Zhuang, L., Williamson, D. F. K., et al. (2022). Artificial intelligence for multimodal data integration in oncology. *Cancer Cell, 40*(10), 1095–1110. https://doi.org/10.1016/j.ccell.2022.09.012

[18] Munquad, S., & Das, A. B. (2023). DeepAutoGlioma: A deep learning autoencoder-based multi-omics data integration and classification tool for glioma subtyping. *BioData Mining, 16*, 32. https://doi.org/10.1186/s13040-023-00349-7