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INTEGRATIVE BIOINFORMATICS ANALYSIS OF GLIOBLASTOMA-ASSOCIATED GENES AND MOLECULAR PATHWAYS

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Abstract:

Glioblastoma is an aggressive and highly malignant brain tumor characterized by rapid growth, widespread infiltration, and considerable genetic heterogeneity. Understanding its molecular basis is critical for identifying new therapeutic targets to improve clinical prognosis. This study employed an integrative bioinformatics approach to investigate glioblastoma-related genes and their molecular pathways using freely available online tools. Disease-associated genes were identified through DisGeNET and explored via protein-protein interaction networks using STRING and GeneMANIA. Functional enrichment and pathway mapping analyses were conducted using Enrichr and Reactome to determine significant biological processes and signaling pathways involved in glioblastoma progression. Hub genes were prioritized based on their frequency of occurrence in interaction networks and enrichment analyses. The analysis highlighted the significance of genes such as EGFR, TP53, PTEN, IDH1, VEGFA, and MGMT, which regulate cell proliferation, apoptosis, angiogenesis, and drug resistance. This study demonstrates the importance of bioinformatics tools in identifying and analyzing critical genes and their networks in glioblastoma, providing insights for in-silico drug discovery.

Keywords: *Bioinformatics, Protein-Protein Interaction, Pathway Analysis, Hub Genes, Drug Targets.*

1. Introduction

Glioblastoma (GBM) is the most frequent and fatal primary malignant brain tumor in adults, responsible for almost 50% of all malignant gliomas (1). Even with advances in neurosurgery, radiation therapy, and chemotherapy, the median survival rate for GBM patients is only 12–15 months (2). The dismal prognosis of GBM can be attributed to its aggressive invasiveness, intratumoral heterogeneity, and low responsiveness to therapy (3). Recent studies on the molecular classification of GBM have identified significant genetic mutations in genes such as EGFR, TP53, PTEN, and IDH1 that are responsible for its progression (4).

The current treatment modalities involve maximum surgical resection followed by radiotherapy and temozolomide-based chemotherapy (2). However, treatment is challenged by recurrence, the blood-brain barrier, and the development of resistance mechanisms such as MGMT-based DNA repair (5). The intricacy of glioblastoma makes it necessary to explore the molecular networks associated with it, as opposed to individual genes (6).

Conventional drug discovery is a costly and time-consuming process, thus necessitating the use of computational approaches (7). Bioinformatics tools have been established as a potential approach for the analysis of genomic data from TCGA and GEO databases (8). Disease-gene association databases such as DisGeNET can be used for the identification of genes associated with glioblastoma (9). Protein interaction tools such as the STRING database and GeneMANIA are useful in the construction of protein networks and the identification of hub genes (10,11). Functional enrichment tools such as Enrichr and biological pathway databases such as Reactome are useful in the biological interpretation of genes (12,13). Hence, the current study uses several bioinformatics tools to identify genes associated with glioblastoma, study molecular interactions, and identify drug targets (14).

Materials and Methods

This study used freely available bioinformatics tools to explore the molecular basis of glioblastoma and to identify important genes and biological pathways that may serve as potential targets for drug discovery. Public databases and online analysis platforms were systematically used to collect, analyze, and interpret genetic information related to glioblastoma. The workflow was carried out in a logical and sequential manner, beginning with disease gene identification and ending with pathway-level interpretation.

Identification of Glioblastoma-Associated Genes using DisGeNET

DisGeNET is a comprehensive disease-gene association database that integrates data from curated biological resources, genome-wide association studies, animal models, and scientific literature. It assigns evidence-based scores to indicate the strength of association between genes and diseases. This tool was used to retrieve genes associated with glioblastoma, which formed the primary dataset for further analysis.

Protein-Protein interaction network construction using STRING

STRING is a protein-protein interaction database that compiles known and predicted interactions derived from experimental studies, curated pathway databases, computational predictions, and text mining. It presents interactions as confidence-scored networks. STRING was used to build a protein-protein interaction network and identify highly connected hub proteins involved in glioblastoma.

Functional network analysis using GeneMANIA

GeneMANIA uses machine-learning algorithms to integrate multiple biological datasets, including gene co-expression, genetic interactions, protein interactions, shared pathways, and co-localization data, to predict gene function and functional associations. This tool was used to expand and validate the interaction network and identify functionally related genes.

Functional enrichment analysis using Enrichr

Enrichr is a gene set enrichment analysis tool that statistically evaluates whether specific biological processes, molecular functions, cellular components, or signaling pathways are significantly associated with a given gene list. Enrichr was used to determine enriched biological functions and cancer-related pathways associated with the selected genes.

Pathway mapping and analysis using Reactome

Reactome is a manually curated and peer-reviewed pathway database that maps genes and proteins to detailed molecular pathways and biological reactions. It supports pathway visualization and over-representation analysis. Reactome was used to map prioritized genes onto curated pathways and understand molecular mechanisms involved in glioblastoma.

Table 1: Bioinformatics Tools Used in the Study

Tool	Working Principle	Application in This Study
DisGeNET	Integrates data from curated databases, GWAS, animal models, and scientific literature to establish disease-gene associations with evidence scores	Used to retrieve genes associated with glioblastoma, forming the primary dataset for further analysis
STRING	Constructs protein-protein interaction networks using experimental data, pathway knowledge, computational predictions, and text mining	Used to build a protein-protein interaction network and identify highly connected hub proteins
GeneMANIA	Uses machine-learning to integrate co-expression, genetic interactions, pathways, and protein interaction data to predict gene function	Used to expand and validate the interaction network and identify functionally related genes
Enrichr	Performs statistical gene set enrichment analysis to identify overrepresented biological processes, molecular functions, and pathways	Used to determine enriched biological functions and cancer-related pathways
Reactome	A manually curated, peer-reviewed database that maps genes and proteins to detailed biological pathways and molecular reactions	Used to map prioritized genes onto curated pathways and understand molecular mechanisms

Results

DisGeNET analysis

Table 2: DisGeNET Summary Table – Glioblastoma (Key Genes)

Gene	Gene Full Name	Variants	Score	PMIDs	First Ref	Last Ref	DisGeNET Score
EGFR	Epidermal growth factor receptor	618	1763	39	1968	2025	0.27
MGMT	O-6-methylguanine-DNA methyltransferase	80	252	103	1992	2025	0.44
PTEN	Phosphatase and tensin homolog	68	216	49	1997	2025	0.30
IDH1	Isocitrate dehydrogenase (NADP+) 1	12	164	52	2003	2025	0.35
VEGFA	Vascular endothelial growth factor A	8	125	41	1992	2025	0.29
CDKN2A	Cyclin dependent kinase inhibitor 2A	67	102	61	1994	2025	0.29
PROM1	Prominin 1	202	130	9	2006	2025	0.39
MET	MET proto-oncogene, receptor tyrosine kinase	156	91	20	1993	2025	0.34
HIF1A	Hypoxia inducible factor 1 subunit alpha	25	122	18	2002	2025	0.33
EGF	Epidermal growth factor	134	82	12	1985	2025	0.33

DisGeNET analysis for glioblastoma identified several genes strongly associated with disease development and progression. The top-ranked genes included EGFR, MGMT, PTEN, IDH1, VEGFA, CDKN2A, PROM1, MET, HIF1A, and EGF, all showing high gene–disease association scores with strong literature support, high evidence scores, and multiple linked variants.

EGFR showed one of the highest association levels with extensive literature support and variants, highlighting its central role in receptor tyrosine kinase signaling and tumor proliferation. MGMT demonstrated strong association supported by high publication counts and chemical interaction data, reflecting its role in DNA repair and resistance to alkylating chemotherapeutic agents such as temozolomide. The tumor suppressor gene PTEN showed strong association supported by high variant counts and evidence scores, as PTEN loss activates the PI3K–AKT signaling pathway contributing to uncontrolled cell growth. IDH1, although having fewer variants, showed a high evidence score reflecting its importance in glioma classification. VEGFA showed strong association with high chemical interaction counts, emphasizing the importance of angiogenesis in glioblastoma.

Additional genes such as CDKN2A, PROM1, and MET support the involvement of cell cycle regulation, cancer stem cell biology, and receptor tyrosine kinase signaling. The presence of HIF1A highlights the role of hypoxia-driven signaling, while EGF supports ligand-mediated activation of EGFR pathways.

STRING Protein-Protein interaction analysis

Protein-protein interaction analysis using STRING revealed a densely interconnected network of glioblastoma-associated genes, indicating strong functional relationships among the selected gene set. The network was centered around EGFR, which appeared as a major hub node with multiple direct interactions with other genes such as PTEN, MET, HIF1A, and EGF.

PTEN formed strong connections with EGFR, IDH1, and CDKN2A, reflecting its role as a critical tumor suppressor regulating the PI3K–AKT signaling pathway. MGMT showed connectivity with CDKN2A, PTEN, and other genes within the network, suggesting functional associations related to DNA repair and treatment resistance. Genes such as MET and PROM1 were well integrated into the network, indicating their involvement in glioblastoma invasiveness and cancer stem cell biology. The presence of HIF1A as an interconnected node highlights the importance of hypoxia-driven signaling.

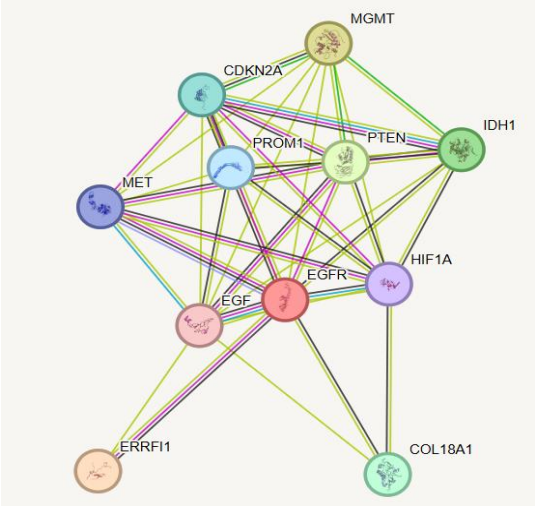

Figure 1: STRING-Derived Protein Interaction Network of Key Glioblastoma Genes

GeneMANIA network analysis

Network analysis using GeneMANIA demonstrated a higher number of functional interaction networks of glioblastoma-related genes, including other genes linked to glioblastoma through co-expression, protein-protein interaction, predicted interaction, and co-localization. The resultant network was densely populated, which shows that there are significant interactions between genes associated with glioblastoma and its interacting partners.In terms of network interaction, physical interactions contributed most to network edges, followed by co-expression and predicted interactions. It shows that a lot of interactions take place at the cellular level between these proteins and their partners due to the high percentage of physical interaction.

Notably, hub genes like EGFR, PTEN, CDKN2A, VEGFA, HIF1A, MET, MGMT, and IDH1 were located in the center of the network with numerous links to their interacting partners. Being located in the center of the network means that these genes play a crucial role in regulating glioblastoma. Other genes identified include HGF, FLT1, ACTB, CAV1, MDM2, ARNT, and E2F8. They are known to be involved in tumor signaling, angiogenesis, cytoskeletal regulation, and cell cycle progression. Interactions centered on EGFR proved highly connected with ligands and downstream regulators, thus emphasizing the importance of EGFR in the process of receptor tyrosine kinase signaling. The module of VEGFA and HIF1A was highly connected and represented a set of interactions typical for hypoxia-driven angiogenesis characteristic for glioblastoma.Among tumor suppressor pathways, one can name PTEN and CDKN2A – both showing multiple physical and genetic connections. These interactions demonstrate the presence of cell cycle checkpoint regulation and apoptosis-related signaling pathway dysregulation in glioblastomas.

The inclusion of MGMT in the network demonstrates that its influence goes beyond the process of DNA repair and involves participation in regulatory networks affecting the course of treatment of the disease. The presence of cytoskeletal and extracellular matrix components also demonstrates the participation of glioblastoma in processes of invasion and microenvironmental remodeling. GeneMANIA network illustrates a complex picture of interactions taking place at different levels – from receptor signaling to tumor-microenvironment interactions and hypoxia response. Prevalence of physical and co-expression interactions demonstrates the organization of regulatory modules in glioblastoma.

Enrichr Functional Enrichment Analysis

Gene Set Enrichment Analysis using Enrichr was used to determine the significantly enriched transcription factors and biological pathways in relation to the given glioblastoma gene set. The analyses were performed through multiple libraries such as Transcription Factor Databases and Reactome Pathways 2024.

1. Transcription factor enrichment analysis

Transcription factor enrichment analysis shows that there is a significant enrichment for certain transcription factors such as TCF3, NFE2L2, SMAD2, RAD21, and HNF4A (ENCODE and ChEA Consensus TFs). This clearly shows that there is a coordinated transcriptional regulation involving the genes present in the glioblastoma gene set. In addition, analysis through the TRRUST Transcription Factors 2019 library showed that there are significant enrichments for SP1, DNMT1, TP53, EGFR, and RELA. TP53 enrichment is due to the known role of p53 as a tumor suppressor gene in glioblastoma, whereas SP1 and DNMT1 enrichment implicates epigenetic and transcription regulation mechanisms during glioblastoma progression. Furthermore, JASPAR PWM analysis shows that there are transcription factor enrichments for E2F2, ZBTB7C, MAFK, NR1D2, and MYBL1. This suggests that there are

also enrichments of cell cycle regulation and oncogenic transcription programs. E2F-related transcription factors show that there is an involvement of cell cycle checkpoint dysregulation in glioblastoma.

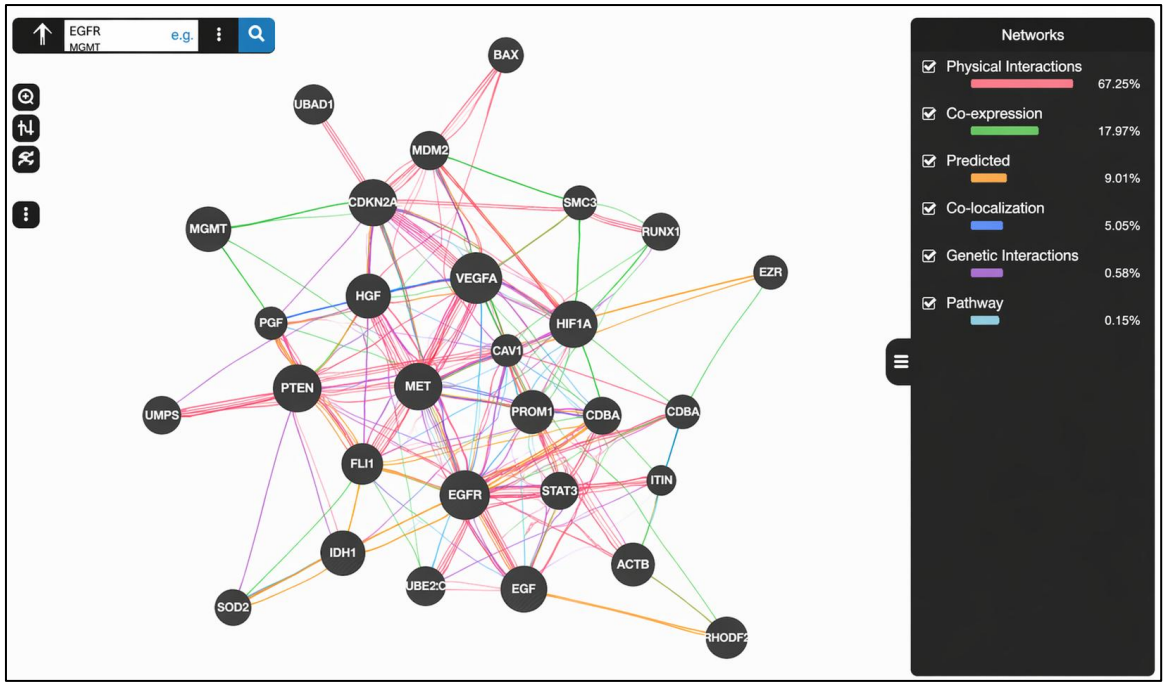

Figure 2: Gene–Gene Interaction Network of Glioblastoma Candidate Genes

2. Reactome pathway enrichment analysis:

The most significantly enriched pathways included:

PI3K–AKT Signaling in Cancer

Negative Regulation of the PI3K–AKT Network

Signaling by Non-Receptor Tyrosine Kinases

Signaling by PTK6

Signaling by Receptor Tyrosine Kinases

PTK6 Promotes HIF1A Stabilization

Inhibition of Signaling by Overexpressed EGFR

Signaling by Overexpressed Wild-Type EGFR in Cancer

PI3K/AKT Activation

EGFR Interacts with Phospholipase C-gamma

The enrichment of PI3K–AKT signaling confirms activation of survival and proliferation pathways consistent with PTEN loss and EGFR amplification. Enrichment of receptor tyrosine kinase signaling pathways highlights the central role of EGFR and MET-mediated signaling. The identification of PTK6-mediated HIF1A stabilization supports the involvement of hypoxia-driven angiogenesis.

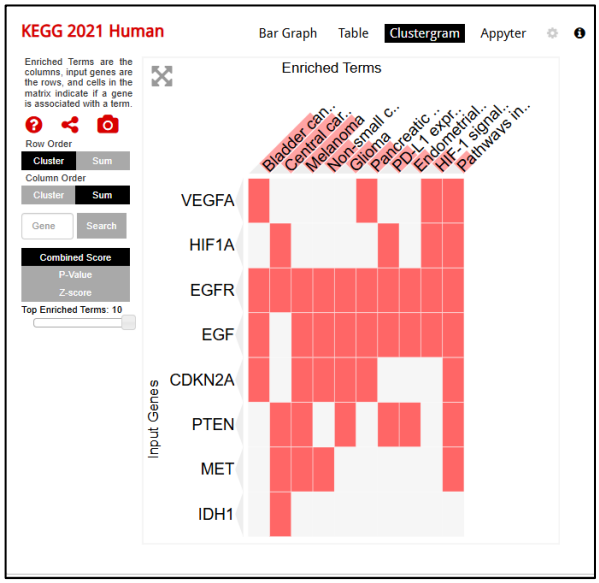

Figure 3: KEGG Pathway Enrichment Clustergram of Glioblastoma-Associated Genes (KEGG 2021 Human)

The Reactome clustergram demonstrates robust clustering of the key genes including EGFR, VEGFA, HIF1A, and EGF in various enriched pathways. In particular, EGFR is found in nearly all of the most enriched pathways, which validates its role as an essential hub gene.Moreover, the genes VEGFA and HIF1A are clustered in the pathways associated with angiogenesis and hypoxia, suggesting co-regulated activity of vascularization mechanisms in glioblastomas.Clustering analysis reveals that the genes do not work individually; instead, they operate in overlapping signal transduction modules, where the hubs include RTK-PI3K-AKT and hypoxia signaling pathways. Enrichr analysis strongly supports the involvement of:

- Receptor Tyrosine Kinase signaling (EGFR/MET axis)
- PI3K–AKT survival pathway activation
- Hypoxia-mediated angiogenesis (HIF1A–VEGF axis)
- Cell cycle dysregulation (E2F-related TFs)
- Epigenetic and transcriptional control mechanisms

The convergence of transcription factor enrichment and pathway enrichment results confirms that glioblastoma progression is driven by coordinated activation of growth factor signaling, angiogenesis, survival signaling, and transcriptional reprogramming.

Reactome pathway mapping

Reactome pathway mapping demonstrated that the mapped genes are predominantly enriched in Signal Transduction pathways, highlighting the central role of receptor tyrosine kinase signaling. Significant clustering was observed in pathways related to Cell Cycle regulation, reflecting the involvement of CDKN2A loss and dysregulation of cell cycle checkpoints.

The genes also map strongly to Programmed Cell Death pathways, suggesting alterations in apoptotic mechanisms. Enrichment in DNA Repair pathways supports the involvement of genomic instability, particularly associated with MGMT-mediated DNA repair and therapeutic resistance. Mapping within Cellular Responses to Stimuli indicates the role of hypoxia-responsive genes such as HIF1A and VEGFA. The involvement of Immune System pathways

suggests potential immune modulation within the glioblastoma microenvironment. Genes mapped under Extracellular Matrix Organization highlight tumor invasion and metastasis.

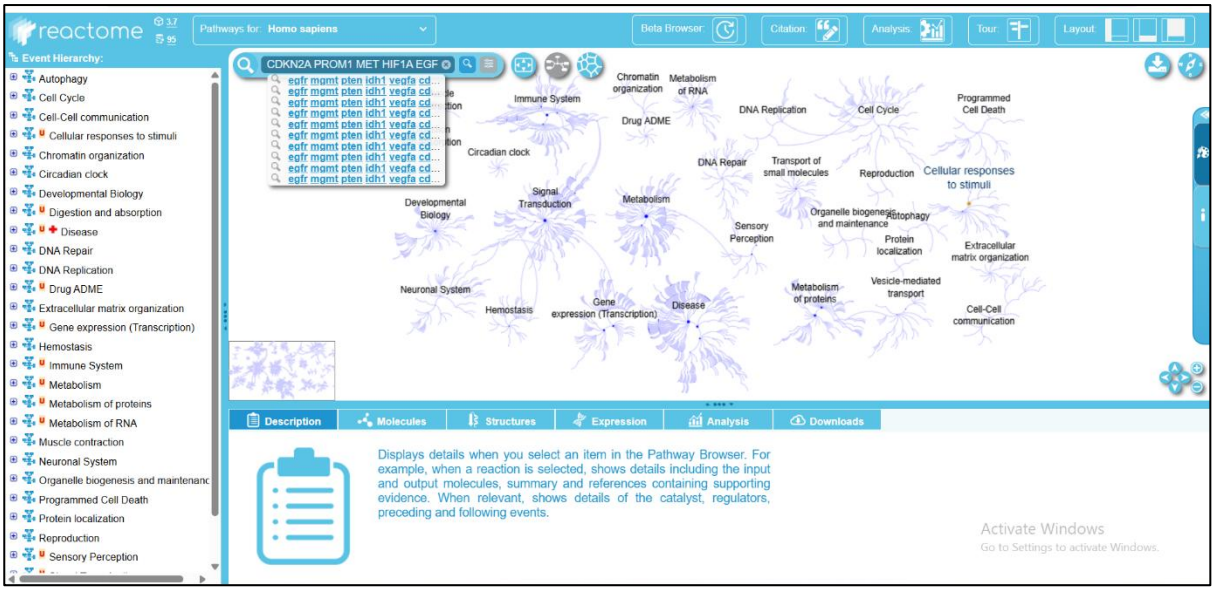

Figure 4: Functional Pathway Landscape of Glioblastoma Genes Using Reactome

Discussion

The current bioinformatics analysis employs gene-disease association, protein interaction, and pathway enrichment approaches to elucidate the molecular basis of glioblastoma (15). The gene-disease association analysis revealed EGFR, PTEN, MGMT, IDH1, VEGFA, CDKN2A, MET, and HIF1A as highly relevant genes, consistent with previous genomic analyses (16). Amplification of EGFR was revealed as a critical molecular event supporting EGFR as a key driver of aberrant receptor tyrosine kinase signaling (17). Loss of PTEN function has been associated with hyperactivation of PI3K/AKT signaling responsible for tumor cell survival, invasion, and therapy resistance (4).

The involvement of the MGMT gene underlined the role of DNA repair in glioblastoma progression and development of resistance to alkylating chemotherapeutic agents (5). The STRING protein interaction network showed a high level of connectivity among the selected genes, indicating their regulation of oncogenic signal cascades (10). Highly interconnected nodes such as EGFR and VEGFA have been identified as hub genes, which may serve as potential biomarkers and therapeutic targets (18).

The GeneMANIA tool provided evidence of gene associations, especially co-expression and pathway interactions in the regulation of the cell cycle and angiogenesis (11). The enrichment of angiogenesis-related genes such as VEGFA and HIF1A underscores the role of hypoxia-mediated tumor vascularization (19). The transcription factor enrichment tool revealed that TP53, SP1, and E2F transcriptional pathways are involved, indicating alterations in cell cycle and tumor suppressor pathways (12). The pathway enrichment analysis revealed PI3K-AKT signaling, receptor tyrosine kinase signaling, and EGFR-mediated pathways, which are hallmark oncogenic pathways in glioblastoma (6).

The Reactome pathway enrichment tool revealed gene involvement in signal transduction, DNA repair, programmed cell death, and immune system pathways, indicating that glioblastoma is a multifactorial

phenomenon (13). The convergence of these pathways underscores that glioblastoma is not caused by a single genetic event but through complex genetic mechanisms involving the interplay of signaling, metabolism, and microenvironmental factors (20). The presence of immune-related pathways points to emerging prospects in glioblastoma immunotherapy (21). The presence of extracellular matrix and invasion-related pathways points to the highly invasive feature of glioblastoma (22).

Conclusion

This study utilized an integrative bioinformatics approach to explore the molecular basis of glioblastoma formation using gene association, protein-protein interaction, and pathway enrichment approaches. The discovery of important glioblastoma-related genes such as EGFR, PTEN, MGMT, IDH1, VEGFA, CDKN2A, MET, and HIF1A reflects the complex genomic profile of the tumor. Protein-protein interaction network analysis showed close functional associations among these genes, indicating coordinated regulation of glioblastoma oncogenic pathways. EGFR and VEGFA were established as hub genes, emphasizing their role as potential diagnostic markers and therapeutic targets.

Functional enrichment revealed significant involvement of receptor tyrosine kinase signaling, PI3K-AKT signaling, angiogenesis, and hypoxia-related pathways. Pathway mapping using Reactome established gene involvement in signal transduction, DNA repair, programmed cell death, and immune system interactions. The findings underscore that glioblastoma development results from complex molecular networks rather than mutations in individual genes. The significance of DNA repair mechanisms such as MGMT in glioblastoma development and the potential for molecular markers in disease management were highlighted. This bioinformatics analysis provides a holistic view of glioblastoma pathogenesis and identifies potential targets for precision medicine approaches.

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References

1. Ostrom, Q. T., Cioffi, G., Waite, K., Kruchko, C., & Barnholtz-Sloan, J. S. (2022). CBTRUS statistical report: Primary brain and other central nervous system tumors diagnosed in the United States. *Neuro-Oncology, 24*(Suppl. 5), v1–v95.
2. Stupp, R., Mason, W. P., van den Bent, M. J., Weller, M., Fisher, B., Taphoorn, M. J., ... & Mirimanoff, R. O. (2005). Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. *New England Journal of Medicine, 352*(10), 987–996.
3. Patel, A. P., Tirosh, I., Trombetta, J. J., Shalek, A. K., Gillespie, S. M., Wakimoto, H., ... & Bernstein, B. E. (2014). Single-cell RNA-seq highlights intratumoral heterogeneity in primary glioblastoma. *Science, 344*(6190), 1396–1401.
4. Cancer Genome Atlas Research Network. (2008). Comprehensive genomic characterization defines human glioblastoma genes and core pathways. *Nature, 455*(7216), 1061–1068.
5. Hegi, M. E., Diserens, A. C., Gorlia, T., Hamou, M. F., de Tribolet, N., Weller, M., ... & Stupp, R. (2005). MGMT gene silencing and benefit from temozolomide in glioblastoma. *New England Journal of Medicine, 352*(10), 997–1003.
6. Hanahan, D. (2022). Hallmarks of cancer: New dimensions. *Cancer Discovery, 12*(1), 31–46.

7. Paul, S. M., Mytelka, D. S., Dunwiddie, C. T., Persinger, C. C., Munos, B. H., Lindborg, S. R., & Schacht, A. L. (2010). How to improve R&D productivity: The pharmaceutical industry's grand challenge. *Nature Reviews Drug Discovery, 9*(3), 203–214.
8. Tomczak, K., Czerwińska, P., & Wiznerowicz, M. (2015). The Cancer Genome Atlas (TCGA): An immeasurable source of knowledge. *Contemporary Oncology, 19*(1A), A68–A77.
9. Piñero, J., Ramírez-Anguita, J. M., Saüch-Pitarch, J., Ronzano, F., Centeno, E., Sanz, F., & Furlong, L. I. (2020). The DisGeNET knowledge platform for disease genomics: 2019 update. *Nucleic Acids Research, 48*(D1), D845–D855.
10. Szklarczyk, D., Gable, A. L., Lyon, D., Junge, A., Wyder, S., Huerta-Cepas, J., ... & Mering, C. V. (2021). STRING v11: Protein–protein association networks with increased coverage. *Nucleic Acids Research, 49*(D1), D483–D489.
11. Warde-Farley, D., Donaldson, S. L., Comes, O., Zuberi, K., Badrawi, R., Chao, P., ... & Morris, Q. (2010). The GeneMANIA prediction server: Biological network integration for gene prioritization and predicting gene function. *Nucleic Acids Research, 38*(Suppl. 2), W214–W220.
12. Kuleshov, M. V., Jones, M. R., Rouillard, A. D., Fernandez, N. F., Duan, Q., Wang, Z., ... & Ma'ayan, A. (2016). Enrichr: A comprehensive gene set enrichment analysis web server 2016 update. *Nucleic Acids Research, 44*(W1), W90–W97.
13. Jassal, B., Matthews, L., Viteri, G., Gong, C., Lorente, P., Fabregat, A., ... & D'Eustachio, P. (2020). The Reactome pathway knowledgebase. *Nucleic Acids Research, 48*(D1), D498–D503.
14. Kuenzi, B. M., & Ideker, T. (2020). A census of pathway maps in cancer systems biology. *Nature Reviews Cancer, 20*(4), 233–246.
15. Louis, D. N., Perry, A., Wesseling, P., Brat, D. J., Cree, I. A., Figarella-Branger, D., ... & Ellison, D. W. (2021). The 2021 WHO classification of tumors of the central nervous system: A summary. *Neuro-Oncology, 23*(8), 1231–1251.
16. Brennan, C. W., Verhaak, R. G., McKenna, A., Campos, B., Noushmehr, H., Salama, S. R., ... & TCGA Research Network. (2013). The somatic genomic landscape of glioblastoma. *Cell, 155*(2), 462–477.
17. Furnari, F. B., Fenton, T., Bachoo, R. M., Mukasa, A., Stommel, J. M., Stegh, A., ... & Cavenee, W. K. (2007). Malignant astrocytic glioma: Genetics, biology, and paths to treatment. *Genes & Development, 21*(21), 2683–2710.
18. Network Medicine was advanced by Barabási, A. L., Gulbahce, N., & Loscalzo, J. (2011). Network medicine: A network-based approach to human disease. *Nature Reviews Genetics, 12*(1), 56–68.
19. Semenza, G. L. (2012). Hypoxia-inducible factors in physiology and medicine. *Cell, 148*(3), 399–408.
20. Hanahan, D., & Weinberg, R. A. (2011). Hallmarks of cancer: The next generation. *Cell, 144*(5), 646–674.
21. Quail, D. F., & Joyce, J. A. (2017). The microenvironmental landscape of brain tumors. *Cancer Cell, 31*(3), 326–341.
22. Winkler, J., Abisoye-Ogunniyan, A., Metcalf, K. J., & Werb, Z. (2020). Concepts of extracellular matrix remodelling in tumour progression and metastasis. *Nature Communications, 11*(1), 5120.