Glioma methylation

Glioma methylation refers to the study of epigenetic modifications, specifically DNA methylation, in gliomas. DNA methylation is a process by which methyl groups are added to the DNA molecule, typically at cytosine-phosphate-guanine (CpG) sites. This modification can affect gene expression without altering the DNA sequence itself, often leading to gene silencing. In the context of gliomas, DNA methylation plays a crucial role in tumor development, progression, treatment response, and prognosis.

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see Methylation status .

see O6 methylguanine DNA methyltransferase.

N6-methylation of adenosine (m6A) is one of the most frequent chemical modifications in eukaryotic RNAs and plays a vital role in tumorigenesis and progression.

Key aspects of glioma methylation research

MGMT Promoter Methylation:

One of the most well-known and clinically relevant methylation markers in glioma is the methylation of the O6-methylguanine-DNA methyltransferase (MGMT) promoter. When the MGMT gene promoter is methylated, the gene is silenced, reducing its ability to repair DNA damage caused by alkylating agents like temozolomide. As a result, gliomas with methylated MGMT promoters are more sensitive to temozolomide chemotherapy and generally have a better prognosis. IDH Mutations and Methylation:

Gliomas with mutations in the isocitrate dehydrogenase (IDH) gene often display a distinct epigenetic profile known as the “glioma CpG island methylator phenotype” (G-CIMP). This phenotype is associated with widespread DNA hypermethylation, which influences tumor behavior and is linked to better clinical outcomes compared to IDH wild-type gliomas. Tumor Suppressor Gene Silencing:

Methylation can lead to the silencing of tumor suppressor genes in gliomas, contributing to tumor initiation and progression. For example, hypermethylation of genes like p16INK4a, RASSF1A, and PTEN has been implicated in glioma pathogenesis. Temozolomide Resistance:

Methylation patterns, especially concerning MGMT, have been extensively studied to understand temozolomide resistance in gliomas. Patients whose tumors lack MGMT promoter methylation are often resistant to temozolomide therapy, necessitating alternative treatment approaches. Immunotherapy and Methylation:

Emerging research is exploring how methylation influences the tumor microenvironment and immune evasion in gliomas. Methylation of genes involved in immune checkpoints or the tumor immune landscape could provide insights for developing immunotherapy strategies. Clinical Relevance:

Prognostic Biomarker: Methylation patterns, such as MGMT promoter methylation, are used to predict treatment response and overall survival in glioma patients. Therapeutic Target: Epigenetic therapies, such as DNA methylation inhibitors, are being investigated to reverse aberrant methylation and improve the efficacy of existing treatments like chemotherapy and immunotherapy. Glioma methylation research continues to be a dynamic field, offering insights into tumor biology, prognosis, and potential therapeutic avenues.

Bibliometric analysis

A study aims to systematically analyze the global trends in glioma methylation research using bibliometric methodologies. We focus on identifying the scholarly trajectory and key research interests, and we utilize these insights to predict future research directions within the epigenetic context of glioma.

Huo et al. performed a comprehensive literature search of the Web of Science Core Collection (WoSCC) to identify articles related to glioma methylation published from January 1, 2004, to December 31, 2023. The analysis included full-text publications in the English language and excluded non-research publications. Analysis and visualization were performed using GraphPad Prism, CiteSpace, and VOSviewer software.

The search identified 3,744 publications within the WoSCC database, including 3,124 original research articles and 620 review articles. The research output gradually increased from 2004 to 2007, followed by a significant increase after 2008, which peaked in 2022. A minor decline in publication output was noted during 2020-2021, potentially linked to the coronavirus disease 2019 pandemic. The United States and China were the leading contributors, collectively accounting for 57.85% of the total research output. The Helmholtz Association of Germany, the German Cancer Research Center (DKFZ), and the Ruprecht Karls University of Heidelberg were the most productive institutions. The Journal of Neuro-Oncology led in terms of publication volume, while Neuro-Oncology had the highest Impact Factor. The analysis of publishing authors revealed Michael Weller as the most prolific contributor. The co-citation network analysis identified David N. Louis's article as the most frequently cited. The keyword analysis revealed “temozolomide,” “expression,” “survival,” and “DNA methylation” as the most prominent keywords, while “heterogeneity,” “overall survival,” and “tumor microenvironment” showed the strongest citation bursts.

The findings of this study illustrate the increasing scholarly interest in glioma methylation, with a notable increase in research output over the past two decades. This study provides a comprehensive overview of the research landscape, highlighting the importance of temozolomide, DNA methylation, and the tumor microenvironment in glioma research. Despite its limitations, this study offers valuable insights into the current research trends and potential future directions, particularly in the realm of immunotherapy and epigenetic editing techniques [1)].

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Huo X, Li H, Xing Y, Liu W, Chen P, Du F, Song L, Yu Z, Cao X, Tian J. Two decades of progress in glioma methylation research: the rise of temozolomide resistance and immunotherapy insights. Front Neurosci. 2024 Sep 2;18:1440756. doi: 10.3389/fnins.2024.1440756. PMID: 39286478; PMCID: PMC11402815.