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MicroRNAs as novel therapeutic agents and focuses in glioblastoma

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INTRODUCTION

Glioblastoma (GBM) is the most aggressive and lethal primary brain tumor in adults. Despite decades of research and clinical efforts, the prognosis for GBM patients remains bleak, with a median survival of only about 15 months. The inherent resistance of GBM to current treatment modalities, including surgery, radiation therapy and chemotherapy, underscores the urgent need for innovative therapeutic strategies. One promising avenue of research in this quest for novel treatments involves microRNAs, small non-coding RNA molecules that play a crucial role in gene regulation. In this article, we explore the potential of microRNAs as both therapeutic agents and targets in the battle against glioblastoma.

DESCRIPTION

MicroRNAs: The tiny regulators

MicroRNAs (miRNAs) are a class of small RNA molecules, typically 20-22 nucleotides in length, that serve as key post-transcriptional regulators of gene expression. They achieve this by binding to the 3' Untranslated Region (3' UTR) of target messenger RNA (mRNA) molecules, leading to either mRNA degradation or translational inhibition. MiRNAs play essential roles in various biological processes, including cell proliferation, differentiation, apoptosis and immune response.

In the context of cancer, aberrant miRNA expression can have profound implications for tumorigenesis and cancer progression. GBM is no exception, with numerous studies demonstrating that specific m iRNAs a re d ysregulated in GBM tissues compared to normal brain tissue. The dysregulated miRNAs in GBM can either act as tumor suppressors or oncogenes, depending on their target genes. Understanding the intricate network of miRNA-mRNA interactions is crucial for unlocking their potential as therapeutic agents and targets.

MicroRNAs as therapeutic agents

Tumor suppressor miRNAs: Several miRNAs have been identified as tumor suppressors in GBM. These miRNAs, when reintroduced or upregulated, can suppress the growth and invasiveness of GBM cells. For example, miR-34a, a well-known tumor suppressor miRNA, has shown promise in preclinical studies as a therapeutic agent. It exerts its

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anti-tumor effects by targeting key oncogenic pathways in GBM, such as the notch and PI3K-Akt signaling pathways.

Oncogene targeting: On the flip side, some miRNAs can promote GBM progression. In these cases, anti-miRNA therapies are being explored. These therapies aim to inhibit oncogenic miRNAs to reduce the proliferation and invasiveness of GBM cells. MiR-21, a well-characterized oncogenic miRNA, is overexpressed in GBM and is associated with poor patient outcomes. Efforts are underway to develop anti-miR-21 therapies to hinder GBM growth.

Sensitivity to conventional treatments: miRNA-based therapies can also enhance the sensitivity of GBM cells to conventional treatments. For instance, miR-182-5p has been found to sensitize GBM cells to radiotherapy, potentially increasing the efficacy of this treatment.

Nanoparticle-based delivery: The successful application of miRNA-based therapies in GBM faces challenges related to delivery to the brain due to the blood-brain barrier. Nanoparticle-based delivery systems, such as lipid nanoparticles and exosomes, are being explored to improve the targeted delivery of miRNA therapies to GBM sites.

MicroRNAs as therapeutic targets

Identifying key players: Beyond using miRNAs as therapeutic agents, understanding which miRNAs are crucial for GBM pathogenesis can guide the development of novel treatment strategies. By identifying miRNAs that are integral to GBM cell survival, proliferation or resistance to treatment, researchers can explore strategies to block or modulate these miRNAs.

Combination therapies: GBM is a complex disease and a single-target therapy may not be sufficient. Combining miRNA-based therapies with traditional treatment modalities, such as temozolomide and radiation therapy or with other emerging therapies, could offer a multi-pronged approach to tackle the disease.

Personalized medicine: GBM is notorious for its heterogeneity, with variations in genetic mutations and miRNA profiles among patients. Personalized medicine approaches, utilizing miRNA profiling to tailor treatment strategies for individual patients, may hold the key to improving outcomes.

Methods to improve miRNA-based therapeutics

miRNA copies and miRNA adversaries are the two different methods to improve miRNA based therapeutics. miRNA mirrors ought to reestablish a deficiency of capability; this miRNA substitution procedure means to once again introduce into malignant growth cells miRNAs that are typically communicated in solid cells yet lost or diminished in tumoral ones. miRNA antagonists ought to restrain endogenous miRNAs that show an increase of capability in unhealthy cells; this procedure is practically identical to other inhibitory therapeutics focusing on a solitary quality item like little particle inhibitors and short meddling RNAs (siRNAs).

Challenges and future directions

While the potential of miRNA-based therapies in GBM is promising, several challenges must be addressed:

Delivery to the brain: Effective delivery of miRNA therapies to the brain remains a major obstacle. Innovative delivery methods, including nanoparticles and viral vectors, must be further developed and tested to ensure specific and efficient delivery to GBM sites.

Off-target effects: miRNA therapies may unintentionally affect other cellular processes, leading to off-target effects. Rigorous preclinical testing and refined delivery strategies are required to mitigate these risks.

Combination therapies: Determining the optimal combinations of miRNA-based therapies with existing treatments or emerging modalities is a complex task that necessitates extensive research and clinical trials.

Regulatory approval: The development of miRNA-based therapies for GBM is still in its early stages. Regulatory approval and clinical translation require substantial investments and a thorough understanding of safety and efficacy profiles.

CONCLUSION

Glioblastoma remains a formidable challenge in the field of oncology and new therapeutic approaches are urgently needed. MicroRNAs, as small but mighty regulators of gene expression, hold great promise in the battle against this aggressive brain cancer. They can serve as both therapeutic agents and targets, offering novel strategies for treatment and potentially improving patient outcomes. However, several hurdles, such as delivery methods and off-target effects, must be overcome to bring miRNA-based therapies to the clinic. As research in this area continues to advance, the hope remains that miRNAs will provide new avenues for GBM treatment, ultimately extending the survival and improving the quality of life for patients battling this devastating disease.