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Potential Biomarkers of Post-traumatic Epileptogenesis: MicroRNAs

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Abstract

Post-traumatic epileptogenesis (PTE) refers to the process by which a traumatic brain injury (TBI) leads to the development of epilepsy. Identifying reliable biomarkers for PTE is crucial for early detection, prognosis, and personalized treatment strategies. MicroRNAs (miRNAs), small non-coding RNAs that regulate gene expression, have emerged as promising candidates for biomarker discovery in PTE. This article provides an overview of the role of miRNAs in PTE and discusses their potential as biomarkers for predicting epileptogenesis following TBI. Key findings from preclinical and clinical studies investigating miRNA expression changes in TBI-induced epileptogenesis are summarized, highlighting their diagnostic and prognostic utility. Furthermore, challenges and future directions in miRNA biomarker research for PTE are discussed, emphasizing the importance of translational efforts to harness the full potential of miRNAs in clinical practice.

Keywords: Post-traumatic epileptogenesis • Biomarkers • MicroRNAs • Traumatic brain injury • Epilepsy

Introduction

Post-Traumatic Epileptogenesis (PTE) is a complex process characterized by the development of epilepsy following a Traumatic Brain Injury (TBI). While not all individuals who experience TBI develop epilepsy, those who do face significant morbidity and mortality. Early detection of individuals at risk for PTE and initiation of preventive strategies are essential for improving outcomes and reducing the burden of epilepsy. Biomarkers play a crucial role in this regard, providing objective measures for predicting epileptogenesis, monitoring disease progression, and guiding treatment decisions. MicroRNAs (miRNAs), small non-coding RNAs that modulate gene expression, have emerged as promising biomarkers for PTE due to their involvement in various pathophysiological processes following TBI. This article provides an overview of the potential role of miRNAs as biomarkers in PTE, summarizing current evidence from preclinical and clinical studies and discussing future directions for translational research [1].

Literature Review

MicroRNAs are small endogenous RNA molecules that regulate gene expression by binding to target messenger RNAs (mRNAs), leading to their degradation or translational repression. Dysregulation of miRNA expression has been implicated in various neurological disorders, including epilepsy. Following TBI, alterations in miRNA expression profiles occur in response to injury-induced changes in cellular signaling pathways, neuroinflammation, synaptic plasticity, and neuronal excitability. Several miRNAs have been identified as key regulators of processes involved in epileptogenesis, such as neuronal hyperexcitability, synaptic remodeling, neuroinflammation, and gliosis. Dysregulated miRNA expression in experimental models of TBI-induced epilepsy suggests their potential involvement in the pathogenesis of PTE and their utility as biomarkers for predicting epileptogenesis [2].

Preclinical studies utilizing animal models of TBI-induced epilepsy have identified specific miRNAs whose expression is altered during epileptogenesis. These miRNAs exhibit dysregulated expression patterns in brain tissue, Cerebrospinal Fluid (CSF), and blood samples following TBI, suggesting their potential as biomarkers for PTE. In clinical studies, differential expression of miRNAs has been observed in TBI patients with and without epilepsy, as well as in individuals with a history of TBI who subsequently develop epilepsy. Moreover, miRNA expression profiles correlate with clinical outcomes, seizure frequency, and response to antiepileptic drugs, highlighting their prognostic and predictive value in PTE. The ability of miRNAs to discriminate between TBI patients at high and low risk for epileptogenesis underscores their potential as non-invasive biomarkers for early detection and personalized management of PTE [3].

Despite promising findings, several challenges must be addressed to facilitate the clinical translation of miRNA biomarkers for PTE. Standardization of experimental protocols, validation of miRNA expression profiles across different patient populations, and establishment of robust analytical methods are essential for ensuring the reproducibility and reliability of miRNA biomarker studies. Furthermore, elucidating the functional roles of dysregulated miRNAs in PTE pathophysiology and developing targeted therapeutic interventions based on miRNA modulation are critical steps towards harnessing the full potential of miRNAs in clinical practice. Multicenter collaborative efforts, longitudinal cohort studies, and integration of multi-omics approaches are needed to advance miRNA biomarker research for PTE and facilitate the development of personalized therapeutic strategies for individuals at risk for TBI-induced epilepsy.

MicroRNAs hold great promise as biomarkers for post-traumatic epileptogenesis, offering insights into disease mechanisms, prognostic information, and opportunities for personalized treatment approaches. Preclinical and clinical studies have identified specific miRNAs whose expression is dysregulated following TBI and correlates with the development of epilepsy. Further research is needed to validate and refine miRNA biomarkers, elucidate their functional roles in PTE pathophysiology, and translate findings into clinical practice. By overcoming challenges and leveraging advances in miRNA biology and analytical techniques, we can harness the diagnostic and prognostic potential of miRNAs to improve outcomes for individuals at risk for post-traumatic epilepsy [4].

Integrating miRNA biomarker research with other omics technologies, such as genomics, transcriptomics, proteomics and metabolomics, holds promise for gaining comprehensive insights into the molecular mechanisms underlying post-traumatic epileptogenesis. Multiomic approaches enable the identification of molecular signatures, pathways, and networks involved in TBI-induced epilepsy, facilitating the discovery of novel biomarkers and therapeutic targets. By integrating miRNA expression data with genomic variations, gene expression profiles, protein abundances, and metabolite concentrations, researchers can elucidate complex regulatory networks and identify converging pathways dysregulated in PTE. Furthermore, multiomic analyses enable the identification of biomarker panels or signatures with improved sensitivity and

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specificity for predicting epileptogenesis, enhancing the diagnostic accuracy and clinical utility of miRNA biomarkers in PTE [5].

Discussion

Non-invasive monitoring of miRNA biomarkers in body fluids, such as blood, saliva, urine, and CSF, enables longitudinal assessment of disease progression and treatment response in individuals at risk for post-traumatic epilepsy. Serial sampling of miRNA expression profiles allows for real-time monitoring of dynamic changes in biomarker levels over time, providing valuable insights into the temporal evolution of epileptogenesis and the efficacy of therapeutic interventions. Non-invasive biomarker monitoring also facilitates the implementation of personalized treatment strategies, allowing for timely adjustments based on individual patient responses and disease trajectories. Longitudinal assessment of miRNA biomarkers in conjunction with clinical outcomes and imaging data enhances the accuracy of prognostic predictions and enables early intervention strategies to mitigate the risk of epilepsy development following TBI.

MicroRNAs implicated in post-traumatic epileptogenesis serve as potential therapeutic targets for the development of novel disease-modifying treatments aimed at preventing or delaying the onset of epilepsy following TBI. Targeting dysregulated miRNAs with specific antagonists or mimics allows for the modulation of gene expression networks involved in epileptogenesis, thereby attenuating neuronal hyper excitability, neuroinflammation, and synaptic dysfunction. Preclinical studies targeting miRNAs associated with PTE have shown promising results in animal models, demonstrating the feasibility and efficacy of miRNA-based therapeutics in mitigating epileptogenesis. Translation of these findings into clinical practice requires rigorous validation of therapeutic targets, optimization of delivery methods, and evaluation of safety and efficacy in human trials. MiRNA-based therapeutics offer a targeted approach for personalized treatment of individuals at high risk for post-traumatic epilepsy, paving the way for precision medicine in TBI-induced epileptogenesis [6].

Conclusion

MicroRNAs represent valuable biomarkers for post-traumatic epileptogenesis, offering insights into disease mechanisms, prognostic information, and therapeutic targets. Integration of miRNA biomarker research with multiomic approaches enables comprehensive profiling of molecular changes underlying TBI-induced epilepsy, facilitating the discovery of novel biomarkers and therapeutic strategies. Non-invasive monitoring of miRNA biomarkers allows for longitudinal assessment of disease progression and treatment response, guiding personalized treatment approaches for individuals at risk for post-traumatic epilepsy. Targeting dysregulated miRNAs holds promise for the development of novel disease-modifying treatments aimed at preventing or delaying the onset of epilepsy following TBI.

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Conflict of Interest

None.

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