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Cutting-edge technologies illuminate the neural landscape of cancer: Insights into tumor development

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Highlights

- Cutting-edge technologies are driving advancements in cancer neuroscience.
- scRNA-seq and imaging reveal CNS tumor origins and TME heterogeneity.
- Schwann cell-TME interactions drive peripheral tumor invasion, metastasis, and pain.
- Cancer therapies remodel the nervous system, worsening neuropathic symptoms.
- Novel target screening integrates sequencing and cross-disciplinary databases.

Abstract

Neurogenesis constitutes a pivotal facet of malignant tumors, wherein cancer and its therapeutic interventions possess the ability to reconfigure the nervous system, establishing a pathologic feedback loop that exacerbates tumor progression. Recent strides in high-resolution imaging, single-cell analysis, multi-omics technologies, and experimental models have opened unprecedented avenues in cancer neuroscience. This comprehensive review summarizes the latest advancements of these emerging technologies in elucidating the biological mechanisms underlying tumor initiation, invasion, metastasis, and the dynamic heterogeneity of the tumor microenvironment(TME), with a specific focus on neuron-glial-tumor interactions in glioblastoma(GBM) and other neurophilic cancers. Moreover, we innovatively propose target screening processes based on sequencing technologies and database frameworks. It rigorously evaluates ongoing clinical trial drugs and efficacy while spotlighting characteristic cells in the central and peripheral TME, consolidating cancer biomarkers pivotal for future targeted therapies and management strategies. By integrating these cutting-edge findings, this review aims to offer fresh insights into tumor-nervous system interactions, establishing a robust foundation for forthcoming clinical advancements.

Introduction

Cancer Neuroscience is an emerging field focused on deciphering the bidirectional interactions between the nervous system and cancer, including the impact of neural invasion on tumor progression and how cancer and its therapies alter and stimulate the nervous system, revolutionizing therapeutic strategies for cancer from a pathophysiological perspective [1].

The nervous system is involved in various aspects of cancer pathophysiology [2]. The central nervous system (CNS) governs the origin, development and metastasis of neurogenic tumors and directly impacts brain tumors, while the peripheral nervous system (PNS) plays a crucial role in

tumor invasion and metastasis [3]. Additionally, tumors and their treatments can have detrimental effects on the nervous system, such as pain, neurological dysfunction, and cognitive impairments [[4], [5], [6], [7], [8]]. Therefore, under the combined influence of synapses, neurotransmitters, and neurotrophic factors, the components and interrelationships within the tumor microenvironment (TME) become increasingly intricate [9]. The significant heterogeneity of the microenvironment further exacerbates the progression, recurrence, and treatment resistance of tumors [8]. Previous research has been constrained by the lack of effective tools to characterize the dynamic properties and overall landscape of these interacting networks, thus limiting a profound understanding of the molecular biology mechanisms. Fortunately, in recent years, emerging technologies have decoded with unprecedented depth and breadth the specific interactions between the nervous system and tumors, visualizing and quantifying the dynamic changes in the TME [[10], [11], [12]]. This has opened up new directions for developing more effective treatment strategies.

Novel imaging techniques facilitate real-time 3D monitoring of tumor dynamics and the interactions between the nervous system and tumors, particularly in glioma invasion, revealing critical sites of interaction and microstructural changes [13]. Single-cell RNA sequencing (scRNA-seq), integrated with multi-omics and spatial transcriptomics (ST), provides insights into cellular heterogeneity, high-resolution molecular networks, and neuron-tumor molecular interactions [14,15]. Additionally, co-culture systems and 3D organoid models bridge experimental and clinical studies, facilitating the analysis of direct cell-cell interactions and cytokine-mediated signaling between tumor and neural cells while also simulating tumor invasion and drug responses [16]. These technologies support the identification of biomarkers, diagnosis and therapeutic targets, accelerating the translation of cancer neuroscience from theory to clinical practice [17]. This review aims to comprehensively update the latest advancements and future research directions in the application of emerging technologies within the field of cancer neuroscience (Supplementary Table S1). It focuses on the biological mechanisms of the nervous system in tumor growth, recurrence, metastasis, and tumor heterogeneity, as well as the reciprocal effects of cancer and its treatment on the nervous system. Additionally, this article innovatively summarizes tumor target screening methods, targeting strategies, adjuvant diagnostics, and clinical monitoring based on emerging technologies, providing new insights for precision medicine and drug development.

Section snippets

Emerging technologies and progress in cancer neurosciences

Cutting-edge technologies are transforming our understanding of tumor complexity and their interactions with the nervous system. Imaging enables early assessment and visualization of neural circuits, while molecular sequencing reveals underlying cellular and molecular mechanisms. Culture models further validate findings and investigate mechanistic details, bridging basic research and clinical translation. In this section, we explore key technological

advancements in cancer neuroscience, ...

Unveiling the biological mechanisms of neural system-driven tumor development with cutting edge technologies

The nervous system governs a broad spectrum of physiological functions and significantly influences the initiation, progression, invasion, and cerebral metastasis of brain tumors [48]. However, the complexity of regulatory mechanisms and the TME has left these biological processes poorly understood. In this section, we focus on the application of emerging technologies in elucidating the role of the nervous system in tumorigenesis, progression, and the formation of heterogeneous ...

Deciphering the impact of cancer and its treatment on the nervous system

As the nervous system is central to cancer pathophysiology, cancer and its therapies can reciprocally influence and reshape the nervous system, establishing pathological feedback loops that drive neuropathic cancer pain, neurological disorders (e.g., epilepsy), and cancer-related cognitive impairment (CRCI) [[4], [5], [6], [7], [8]]. Therefore, exploring these mechanisms through cutting-edge technologies can enhance our understanding of the pathogenesis of neurological complications and guide ...

Auxiliary clinical and preclinical research

In the preceding text, we have elucidated in detail the novel biological mechanisms underlying tumor progression from an interdisciplinary perspective. The in-depth exploration of these mechanisms not only offers a fresh perspective on the intricate interactions between tumors and the nervous system but also gives rise to a novel approach to target selection and more refined targeting strategies. Furthermore, the progress of these technologies has introduced effective tools that can be ...

Challenges and opportunities

The integration and application of multimodal technologies in cancer neuroscience have greatly accelerated the analysis of neuro-tumor interaction mechanisms, revealing the molecular foundation of neurooncology from various perspectives, though it also presents multiple challenges and opportunities [200,201]. In terms of imaging technologies, while MRI can macroscopically analyze the spatial relationship between tumors and nerves, its spatial and temporal resolution (>100μm) makes it difficult ...

Conclusions and future perspectives

The emerging field of cancer neuroscience has redefined tumor biology, unveiling the critical role of the nervous system in cancer initiation and progression, while exploring the impact of

cancer and its treatments on neurological function [48]. This review summarizes recent advances and emerging technologies applied in this field, emphasizing the significant role of these technologies in elucidating biological mechanisms, as well as in clinical and preclinical research.

High-resolution imaging …

CRediT authorship contribution statement

Yajing Wang: Writing – review & editing, Writing – original draft, Visualization, Supervision. **Zhaojun Wang:** Writing – review & editing, Writing – original draft, Visualization, Supervision. **Xinyuan Mao:** Writing – review & editing, Writing – original draft, Visualization, Supervision. **Hongrui Zhang:** Writing – review & editing, Writing – original draft, Visualization, Supervision. **Lu Zhang:** Writing – review & editing, Supervision. **Yufei Yang:** Writing – review & editing, Visualization, …

Availability of data and materials

Not applicable. …

Declarations

Not applicable. …

Ethical approval and consent to participate

Not applicable. …

Consent for publication

Not applicable. …

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal

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1 The authors contributed equally to this work.

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