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The Role of Kinase Inhibitors in Cancer Neuroscience: Mechanisms, Therapeutic Potential, and Future Directions

Manos C Vlasiou [1]

Affiliations

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Abstract

Introduction: Cancer progression is increasingly understood to be influenced by neural mechanisms, including neurotransmitter signaling, neurotrophic factor activity, neuroinflammation, and neurogenic inflammation. These neurobiological interactions contribute to tumor proliferation, angiogenesis, and metastasis. Kinase inhibitors, a class of targeted therapies that block dysregulated kinase activity, have demonstrated promise not only in direct tumor suppression but also in modulating neural pathways associated with cancer progression.

Methods: This review examines the role of kinase inhibitors in modulating cancer-associated neural mechanisms. A comprehensive literature search was conducted to identify studies exploring the effects of kinase inhibition on: (1) neurotransmitter signaling pathways; (2) neurotrophic factors such as nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF); (3) neuroinflammation through glial cell modulation; and (4) neurogenic inflammation. Additionally, we assessed the impact of kinase inhibitors on tumor-induced axonogenesis and stress-related signaling. Clinical relevance was evaluated through analysis of preclinical models, human case studies, and outcomes from relevant clinical trials.

Results: Kinase inhibitors were found to significantly modulate neural factors that facilitate tumor growth. Specifically, they can suppress neurotrophic signaling (e.g., NGF/TrkA, BDNF/TrkB), inhibit glial activation, reduce pro-inflammatory cytokine production, and block neurotransmitter-induced proliferation. Inhibition of stress-responsive kinases such as p38 MAPK and JNK also disrupted tumor-associated axonogenesis and inflammation. Clinical trials demonstrate improved outcomes in cancers such as glioblastoma, breast cancer, and pancreatic cancer when kinase inhibitors are employed with consideration of neural mechanisms.

Discussion: These findings support the emerging concept of targeting the neural tumor microenvironment as a therapeutic strategy. Kinase inhibitors represent a dual-action approach, suppressing both cancer cell intrinsic growth pathways and the neural factors that sustain them. However, several challenges persist, including resistance mechanisms, variability in patient neural profiles, and off-target effects. Future research should focus on the development of neural-specific kinase inhibitors, the use of neural biomarkers for therapy selection, and the integration of neuro-oncology into personalized treatment plans.

Conclusion: Kinase inhibitors offer a promising frontier in cancer treatment by targeting neural mechanisms that contribute to tumor progression. While current evidence is encouraging, further investigation is required to optimize their use within neuro-oncology. Personalized approaches and novel targets within the neural-cancer axis will be essential for translating this strategy into clinical practice and improving long-term patient outcomes.