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LETTER TO THE EDITOR

Unlocking the Potential of AI: Development of BRAF Inhibitors for Ameloblastomas

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Ameloblastoma is a benign odontogenic tumor characterized by a slow growth rate but notable for its locally aggressive behavior and high recurrence rate (Effiom et al. 2018). Studies have highlighted recurrent somatic mutations in the mitogen-activated protein kinase (MAPK) pathway, particularly the BRAFV600E mutation, in ameloblastomas (Anbinselvam et al. 2024). This same mutation is observed in other malignancies, such as melanoma and thyroid cancer, where targeted therapies using BRAF inhibitors have demonstrated remarkable clinical efficacy (Chen et al. 2023).

In this context, we discuss the potential application of artificial intelligence (AI) in predicting and developing novel BRAF inhibitors for ameloblastoma treatment. AI has revolutionized healthcare by advancing disease diagnosis, clinical decision-making, medical imaging, and drug discovery (Hillary et al. 2024). The drug development process is inherently complex, requiring extensive time, resources, and rigorous preclinical and clinical testing to ensure safety and efficacy (Yang & Kar 2023). However, AI, particularly machine learning, enables the integration and analysis of large datasets, accelerating problem-solving and facilitating breakthroughs in drug discovery (Yang & Kar 2023). For ameloblastomas, AI-driven methods could offer a more personalized treatment strategy, particularly for tumors containing the BRAFV600E mutation.

BRAF-positive tumors often exhibit aggressive behavior, an increased risk of recurrence, and resistance to apoptosis (Fregnani et al. 2017). While some studies suggest that the BRAFV600E mutation does not significantly affect the progression of ameloblastomas, early reports on BRAF inhibitors, such as dabrafenib and vemurafenib, have shown promising results (Ebeling et al. 2023, Martins-de-Barros et al. 2024).

Resistance to BRAF inhibitors is often driven by genetic and non-genetic mechanisms, including the formation of BRAF homodimers, hyperactivation of MEK within the MAPK pathway, and activation of alternative signaling pathways such as PI3K/AKT (Proietti et al. 2020). Furthermore, the loss of the tumor suppressor PTEN has been linked to resistance mechanisms (Proietti et al. 2020). These alterations underscore the need for innovative therapeutic strategies, such as combination therapies

(e.g., BRAF inhibitors with MEK inhibitors), next-generation BRAF inhibitors, and novel immunotherapy approaches (Zhong et al. 2022).

Alternatively, AI could play a pivotal role in addressing these challenges. Tools like AlphaFold, a neural network-based model for protein structure prediction, have already demonstrated remarkable accuracy in predicting protein folding from amino acid sequences (Yang et al. 2023). This technology has shown potential in peptide based drug discovery, offering critical insights into novel compounds' physicochemical properties and toxicity profiles (Gupta et al. 2021). By leveraging AI-driven platforms, researchers can accelerate the design of next-generation BRAF inhibitors tailored to ameloblastomas, potentially overcoming resistance mechanisms and enhancing clinical outcomes. Through murine models, these drugs can be preliminarily evaluated for their safety and efficacy in a therapeutic context (Guo et al. 2024).

In conclusion, developing AI-designed BRAF inhibitors offers a novel avenue for improving the treatment of ameloblastomas. Future studies should prioritize validating these approaches, exploring combination therapies, and incorporating AI into clinical workflows to enhance therapeutic efficacy and minimize resistance. The synergy between AI, oncology, and pharmacology holds the potential to transform the management of ameloblastomas and other challenging tumors, ultimately improving patient care and outcomes.

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