Curr Neuropharmacol. 2023 Aug 15. doi: 10.2174/1570159X21666230809110444.
Online ahead of print.

Targeting Histone 3 Variants Epigenetic Landscape and Inhibitory Immune Checkpoints: An Option for Paediatric Brain Tumours Therapy

Sarasa Meenakshi [1], Krushna Ch Maharana [2], Lokesh Nama [2], V Udaya Kumar [1], Sameer Dhingra [1], Velayutham Ravichandiran [1], Krishna Murti [1], Nitesh Kumar [2]

Affiliations

PMID: 37605389 DOI: 10.2174/1570159X21666230809110444

Abstract

Despite little progress in survival rates with regular therapies, which do not provide complete care for curing pediatric brain tumors (PBTs), there is an urgent need for novel strategies to overcome the toxic effects of conventional therapies to treat PBTs. The co-inhibitory immune checkpoint molecules, e.g., CTLA-4, PD-1/PD-L1, etc., and epigenetic alterations in histone variants, e.g., H3K27me3 that help in immune evasion at tumor microenvironment have not gained much attention in PBTs treatment. However, key epigenetic mechanistic alterations, such as acetylation, methylation, phosphorylation, sumoylation, poly (ADP)-ribosylation, and ubiquitination in histone protein, are greatly acknowledged. The crucial checkpoints in pediatric brain tumors are cytotoxic T lymphocyte antigen-4 (CTLA-4), programmed cell death protein-1 (PD-1) and programmed death-ligand 1 (PDL1), OX-2 membrane glycoprotein (CD200), and indoleamine 2,3-dioxygenase (IDO). This review covers the state of knowledge on the role of multiple co-inhibitory immunological checkpoint proteins and histone epigenetic alterations in different cancers. We further discuss the processes behind these checkpoints, cell signalling, the current scenario of clinical and preclinical research and potential futuristic opportunities for immunotherapies in the treatment of pediatric brain tumors. Conclusively, this article further discusses the possibilities of these interventions to be used for better therapy options.

Keywords: Epigenetics; cell signalling.; histones; immune checkpoints; immunotherapy; pediatric brain tumor.