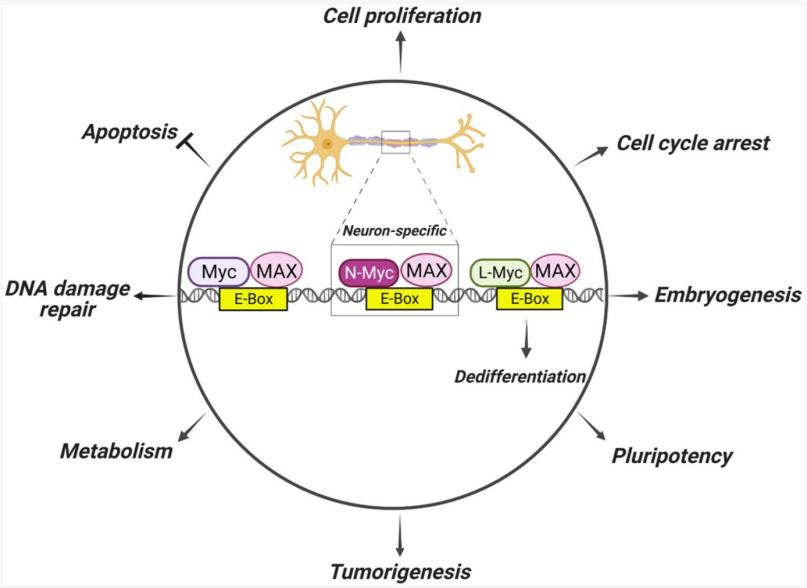
MYCN and MDM2: A Transformative Strategy in Cancer Therapy

CHONGQING , CHONGQING , CHINA, January 29, 2025 /EINPresswire.com/ -- Over the past two decades, the idea of targeting transcription factors to combat malignancies has turned into a clinical reality. Targeting oncogenes and their interactive partners is an effective approach to developing novel targeted therapies for cancer and other chronic diseases. The MYC family of proteins, which are transcription factors, play a pivotal role in many cellular processes. However, dysregulation of MYC, such as amplification of MYCN, is associated with tumorigenesis, especially for neuroblastoma. MDM2, on the other hand, is one of the most frequently studied oncogenes and is an excellent target for cancer therapy, based on its p53-dependent and p53-independent oncogenic activities in various cancers.



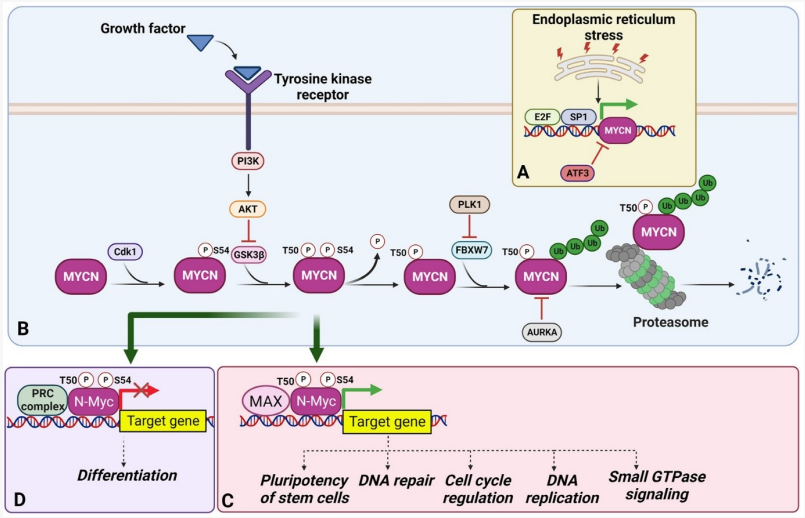
The Myc family of transcription factors, including Myc, N-Myc, and L-Myc, bind DNA at specific sequences and regulate gene expression by binding to enhancer-box (E-Box) sequences via dimerization with Myc-associated factor X (MAX). Downstream gene express

This comprehensive review published in the Genes & Diseases journal by a team from the Department of Pharmacological and Pharmaceutical Sciences, College of Pharmacy, and Drug Discovery Institute, University of Houston focuses on the oncogenic properties of MYCN and its molecular regulation and encapsulates the major therapeutic strategies being developed based on preclinical findings. This review also highlights the potential benefits of targeting both the MYCN and MDM2 oncogenes, providing preclinical evidence of the efficacy and safety of this approach.

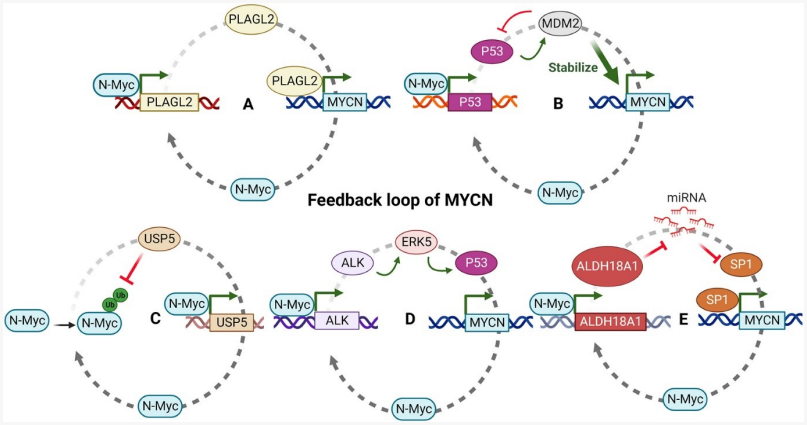
As a key survival signaling pathway, the MDM2/p53 axis is widely involved in the development of many tumors. Preclinical and clinical trials provide evidence to support the notion that inhibition of MDM2 could be a potential therapeutic approach for neuroblastoma. Furthermore, the

concept of dual-targeted inhibition, which effectively restrains both MYCN and MDM2, along with other critical molecules in neuroblastoma progression, presents an intriguing strategy. Since there is a positive feedback loop between MYCN and MDM2, targeting MDM2 would inhibit both MYCN-mediated tumorigenesis and MDM2-regulated survival of neuroblastoma cells. MYCN and MDM2 inhibition has gained attention not only in neuroblastoma but also in a spectrum of other cancer types due to their potential in targeting key oncogenic pathways. Thus, the exploration of synergistic combination therapies, encompassing targeted agents, immunotherapies, and conventional treatments, remains paramount in achieving maximal therapeutic outcomes while minimizing resistance.

The authors emphasize that with continued research, innovative strategies, and a commitment to addressing the complexities of cancer biology, the future holds the promise of transformative breakthroughs in cancer therapy. In conclusion, the development of effective small molecules that inhibit both MYCN and MDM2 represents a promising new strategy for the treatment of neuroblastoma and other cancers.



(A) Transcription factors such as E2 promoter binding factor (E2F) and specific protein 1 (SP1) can directly increase the expression of MYCN, while activating transcription factor 3 (ATF3) reduces MYCN expression. (B) Several kinases activate the transcri



MYCN and its target genes form several feedback loops, playing important roles in regulating MYCN expression and function in tumorigenesis. (A) Pleiomorphic adenoma gene-like 2 (PLAGL2) is a transcription factor that directly activates the transcription o

Reference

Title of Original Paper Targeting the MYCN-MDM2 pathways for cancer therapy: Are they druggable?

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