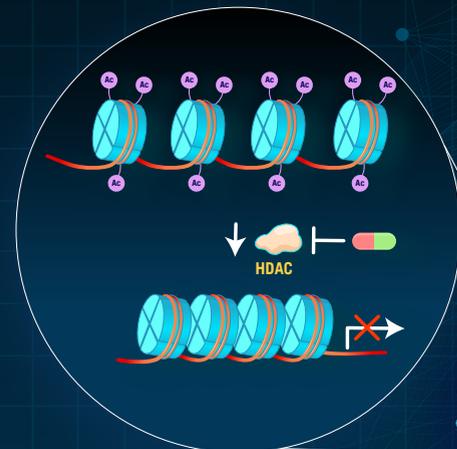


EPIGENETIC CANCER THERAPY: TARGETS AND STRATEGIES

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Epigenetic events shape cancer initiation and progression. By targeting mechanisms involved in epigenetic regulation, epigenetic therapeutics serve as effective weapons against cancer.

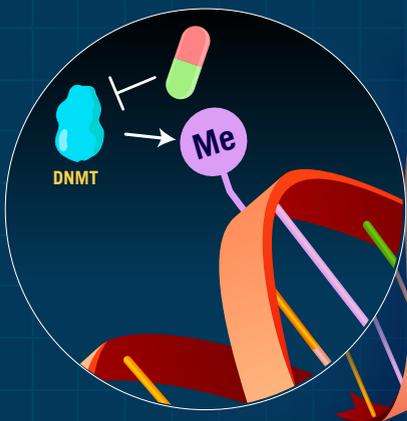


Inhibiting histone deacetylation

Histone deacetylases (HDACs) remove acetyl groups from histone lysine residues, leading to closed chromatin structures and gene silencing. HDAC mutations aberrantly deacetylate or inactivate tumor suppressor genes that slow cell division, promoting cancer development (1). HDAC inhibitor drugs upregulate tumor suppressor genes and inhibit cancer cell growth.

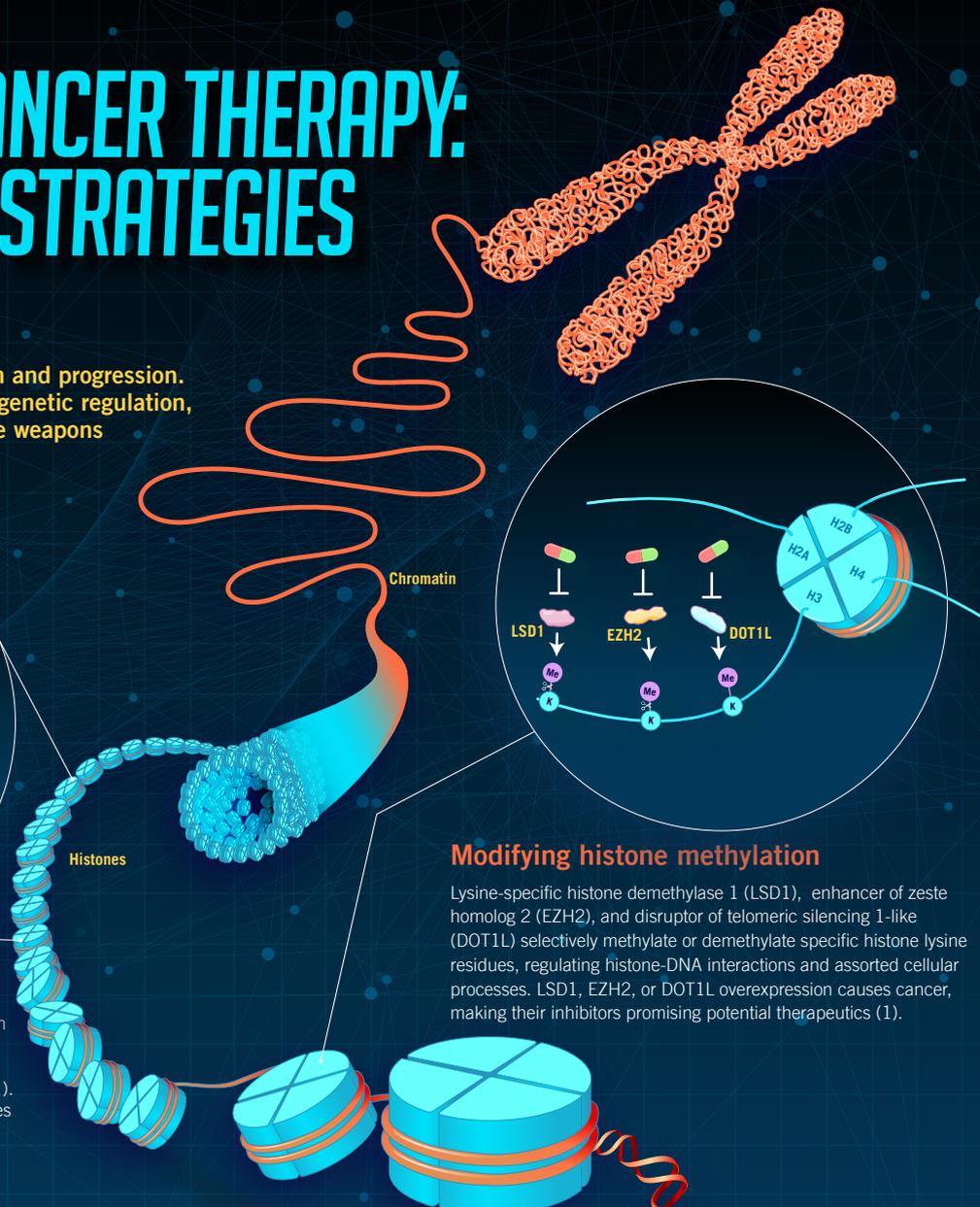
Targeting DNA methylation

DNA methylation by DNA methyltransferases (DNMTs) blocks transcriptional factor binding and disrupts gene activity, triggering many cancer types. DNMT blockade drugs effectively prevent DNA hypermethylation and inhibit tumor progression (2)



References

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- Hu, C., Liu, X., Zeng, Y., Liu, J. & Wu, F. DNA methyltransferase inhibitors combination therapy for the treatment of solid tumor: mechanism and clinical application. *Clinical Epigenetics* 13, 166 (2021).
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Modifying histone methylation

Lysine-specific histone demethylase 1 (LSD1), enhancer of zeste homolog 2 (EZH2), and disruptor of telomeric silencing 1-like (DOT1L) selectively methylate or demethylate specific histone lysine residues, regulating histone-DNA interactions and assorted cellular processes. LSD1, EZH2, or DOT1L overexpression causes cancer, making their inhibitors promising potential therapeutics (1).

Changing RNA modification

As critical epigenetic modulators, noncoding RNAs undergo methylation modification mediated by methyltransferase-like protein 3 (METTL3), affecting RNA structures and functions. Changes to RNA methylation machinery influence tumor cell proliferation and differentiation (3). Reversing abnormal RNA methylation by targeting METTL3 represents a novel approach to cancer treatment.

