Histone methyltransferase

Histone methyltransferases (HMT) are histone-modifying enzymes, (including histone-lysine N-methyltransferase and histone-arginine N-methyltransferase), that catalyze the transfer of one, two, or three methyl groups to lysine and arginine residues of histone proteins. The attachment of methyl groups occurs predominantly at specific lysine or arginine residues on histones H3 and H4.

Two major types of histone methyltranferases exist, lysine-specific (which can be SET (Su(var)3-9, Enhancer of Zeste, Trithorax) domain containing or non-SET domain containing) and arginine-specific.

In both types of histone methyltransferases, cofactor S-Adenosyl methionine (SAM) serves as a cofactor and methyl donor group.

In eukaryotic cells, the genome is tightly condensed into chromatin (composed of DNA and histone proteins, so enzymes, such as histone methyltransferases, must overcome this inaccessibility.

Histone methyltransferase does so by modifying histones at certain sites through methylation. Methylation of histones is important biologically because it is the principal epigenetic modification of chromatin that determines gene expression, genomic stability, stem cell maturation, cell lineage development, genetic imprinting, DNA methylation, and cell mitosis.

Experimental data implicates histone H3 lysine (K) methyltransferases SETDB1 and SUV39H1 into glioma pathobiology, whereas linker histone variant H1.0 and H4K20me3 reportedly affect prognosis. Sepsa et al. investigated the expression of H3K9me3 and its methyltransferases along with H4K20me3 and H1x in 101 astrocytic tumors with regard to clinicopathological characteristics and survival. The effect of SUV39H1 inhibition by chaetocin on the proliferation, colony formation and migration of T98G cells was also examined. SETDB1 and cytoplasmic SUV39H1 levels increased from normal brain through low-grade to high-grade tumors, nuclear SUV39H1 correlating inversely with grade. H3K9me3 immunoreactivity was higher in normal brain showing no association with grade, whereas H1x and H4K20me3 expression was higher in grade 2 than in normal brain or high grades. These expression patterns of H1x, H4K20me3 and H3K9me3 were verified by Western immunoblotting. Chaetocin treatment significantly reduced proliferation, clonogenic potential and migratory ability of T98G cells. H1x was an independent favorable prognosticator in glioblastomas, this effect being validated in an independent set of 66 patients. Diminished nuclear SUV39H1 expression adversely affected survival in univariate analysis. In conclusion, H4K20me3 and H3K9 methyltransferases are differentially implicated in astroglial tumor progression. Deregulation of H1x emerges as a prognostic biomarker [1)]

1)

Sepsa A, Levidou G, Gargalionis A, Adamopoulos C, Spyropoulou A, Dalagiorgou G, Thymara I, Boviatsis E, Themistocleous MS, Petraki K, Vrettakos G, Samaras V, Zisakis A, Patsouris E, Piperi C, Korkolopoulou P. Emerging Role of Linker Histone Variant H1x as a Biomarker with Prognostic Value in Astrocytic Gliomas. A Multivariate Analysis including Trimethylation of H3K9 and H4K20. PLoS One. 2015 Jan 20;10(1):e0115101. doi: 10.1371/journal.pone.0115101. eCollection 2015. PubMed PMID: 25602259.