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Histone Mutations in Cancer

Recent studies show that recurrent somatic mutations in histones (Oncohistones) especially in histone H3 are key drivers in various cancers, including pediatric glioblastoma and soft tissue sarcoma, brain tumors, chondroblastoma, head and neck squamous cell carcinoma, giant cell tumors of bone, and leukemia.

Methods to detect the oncohistones could help in diagnostic and prognostic applications and further the efforts toward targeted therapy. Scientists are already taking advantage of this knowledge to test drugs either targeting the mutation or its consequences.

Overview of five common mutations in histone H3 - 27M, 36M and G34 (R/V/W)

H3K27M is found in 30% of pediatric high-grade glioblastoma (pHGG) and in 80% of diffuse intrinsic pontine glioma (DIPG), and associated with mutations in TP53, PDGFRA, ACVR1, and BCOR. This mutation is also implicated in adult cancers such as glioma, acute myeloid leukemia and melanoma. H3K27M leads to reduced H3K27 methylation, increase in H3K27ac and DNA hypomethylation, and consequently to gene activation with EZH2 inhibition by a negative-dominant effect.

H3K36M is detected in 95% of chondroblastoma, and at lower frequency in pediatric soft tissue carcinoma, head and neck squamous cell carcinoma, melanoma, bladder, and colorectal cancer. H3K36M has a dominant-negative effect on H3K36me2/3, inhibiting the activity of SETD2 and interfering with H3K27 methylation.

H3G34 mutation is found in children and young adult tumors where it is frequently substitute to R or V. H3G34R/V was shown to be correlated with ATRX/DAXX mutation in pHGG. H3G34W and H3G34L mutation is found mostly in the H3F3A gene in 90% of giant cell tumors of bone. H3G34W increases the proliferative and migration capacities of these benign tumors and impairs osteogenic differentiation.

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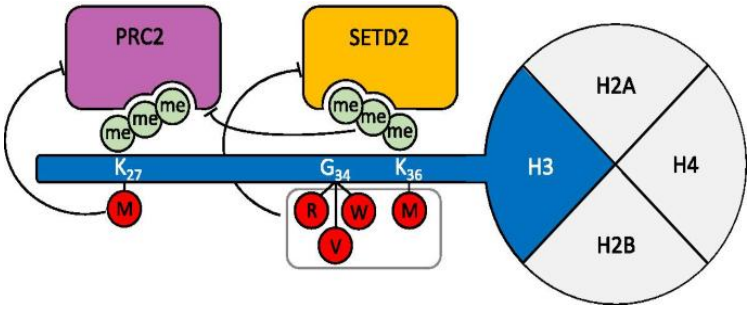
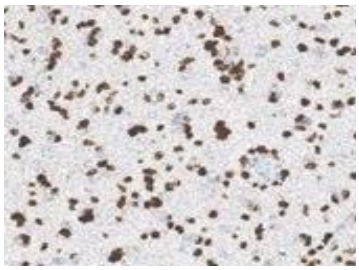
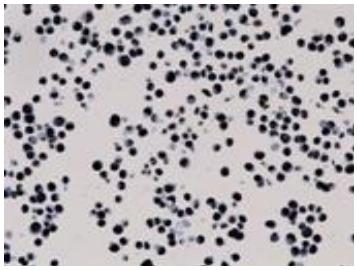


Proposed mechanisms of the main histone H3 mutations. H3K27M leads to a loss of H3K27me3 and H3K27me2 by acting as a dominant-negative inhibitor of PRC2, the complex responsible for H3K27 methylation. H3K36M oncohistone binds and dominantly inhibits the activity of SETD2, the histone methyltransferase responsible for H3K36 methylation. Methylation of H3K36 is known to antagonize the function of PRC2. H3G34 mutants block SETD2 binding, thus reducing its activity on H3K36 methylation. Mutations are indicated in red circles; methyl groups are shown as green circles.

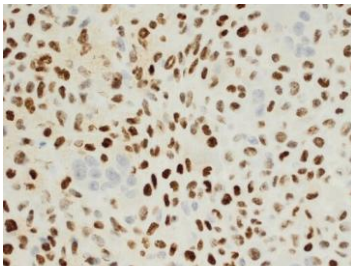
The dark side of histones: genomic organization and role of oncohistones in cancer.
Stefano Amatori, et al. Clinical Epigenetics volume 13, 71, 2021



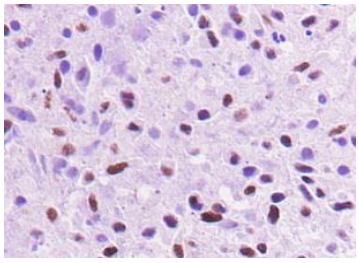
FFPE human brain tumor stained with anti-H3K27M [RM192]



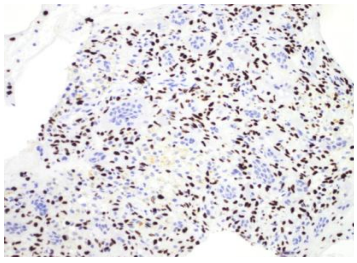
FFPE HepG2 cells stained with anti-H3K27Me3 [MD48R]



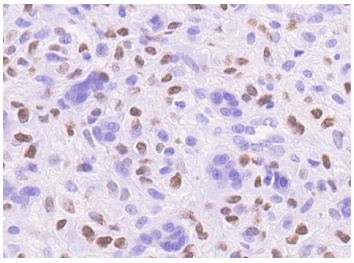
FFPE Chondroblastoma stained with anti-H3K36M [RM193]



FFPE human giant cell tumor stained with anti-H3G34R [MD257R]



FFPE human GCBT stained with anti-H3G34W [RM263]



FFPE human giant cell tumor stained with anti-H3G34V [MD258R]

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Oncohistone Antibodies

Catalog No.	Name	Clone	Host	Volume
MC0051	Histone H1 (Nuclear Marker) [AE-4]	AE-4	Mouse	1 ml
RM0118	Histone H3 Acetyl Lys27/H3K27ac [MD162R]	MD162R	Rabbit	1 ml
RM0116	Histone H3 Acetyl Lys9/H3K9ac [MD161R]	MD161R	Rabbit	1 ml
RM0084	Histone H3 Family 3A/H3F3A [MD148R]	MD148R	Rabbit	1 ml
RM0106	Histone H3 K27M Mutant/H3K27M [RM192]	RM192	Rabbit	1 ml
RM0207	Histone H3 K36M Mutant/H3K36M [RM193]	RM193	Rabbit	1 ml
RM0464	Histone H3 Phospho (PHH3) (pSer10) [MD111R]	MD111R	Rabbit	1 ml
RM0464RTU7	Histone H3 Phospho (PHH3) (pSer10) [MD111R]	MD111R	Rabbit	7 ml
RC0305	Histone H3 Phospho (PHH3) Polyconal	Polyclonal	Rabbit	1 ml
RC0305RTU7	Histone H3 Phospho (PHH3) Polyconal	Polyclonal	Rabbit	7 ml
RM0115	Histone H3 Tri-Methyl Lys27/H3K27Me3 [MD48R]	MD48R	Rabbit	1 ml
RC0185	Histone H3 Tri-Methyl Lys9/H3K9Me3 Polyclonal	Polyclonal	Rabbit	1 ml
RM0222	Histone H3 G34R Mutant/H3G34R [MD257R]	MD257R	Rabbit	1 ml
RM0223	Histone H3 G34V Mutant/H3G34V [MD258R]	MD258R	Rabbit	1 ml
RM0211	Histone H3 G34W Mutant/H3G34W [RM263]	RM263	Rabbit	1 ml
RC0279	Histone H4/H4M/HIST1H4A Polyclonal	Polyclonal	Rabbit	1 ml

Research Use Only

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