

ONCOHISTONES

By:

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Oncohistones are recurrent somatic Mutations in the Histone Gene, Histone H3

This drives oncogenes

Histones are proteins around which DNA is wrapped to form chromatin

Oncohistones Mutations disrupt the normal functions

These Oncohistones Mutations are seen in

- 1 Pediatric high grade glioma
- 2 Giant Cell Tumors of Bone
- 3 Chondroblastomas

Oncohistones are important in diagnosis by

IHC

and targeted therapy

Types of Histones

H2A

H2B

H3

H4 and

H1 linker Histone

For the Bone tumors

Giant Cell Tumor of Bone

H3.3G34W

is used

In IHC the Mononuclear Stromal cells are stained .

It is a nuclear stain

The Giant cells are not stained

This has shown high sensitivity and specificity

It is used to diagnose Giant Cell Tumors of the Bone in small biopsies and to differentiate GCT B from other Giant cell containing lesions

This H3.3G34W Staining is seen in the Malignant GCT B ,Metastatic GCT B.and Post denosumab GCT B

It is useful in small volume biopsies

To differentiate GCT B from the mimics

For

Chondroblastoma

H3K36M. IHC

is used .

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Oncohistones

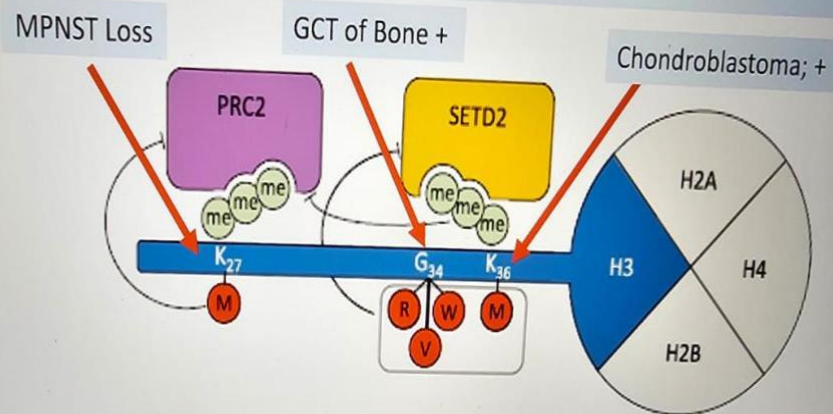


Fig. 3 Proposed mechanisms of the main histone H3 mutations. H3K27M leads to a loss of H3K27me3 and H3K27me2 by acting as a dominant-negative inhibitor of PRC2, the complex responsible for H3K27 methylation. H3K36M oncohistone binds and dominantly inhibits the activity of SETD2, the histone methyltransferase 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