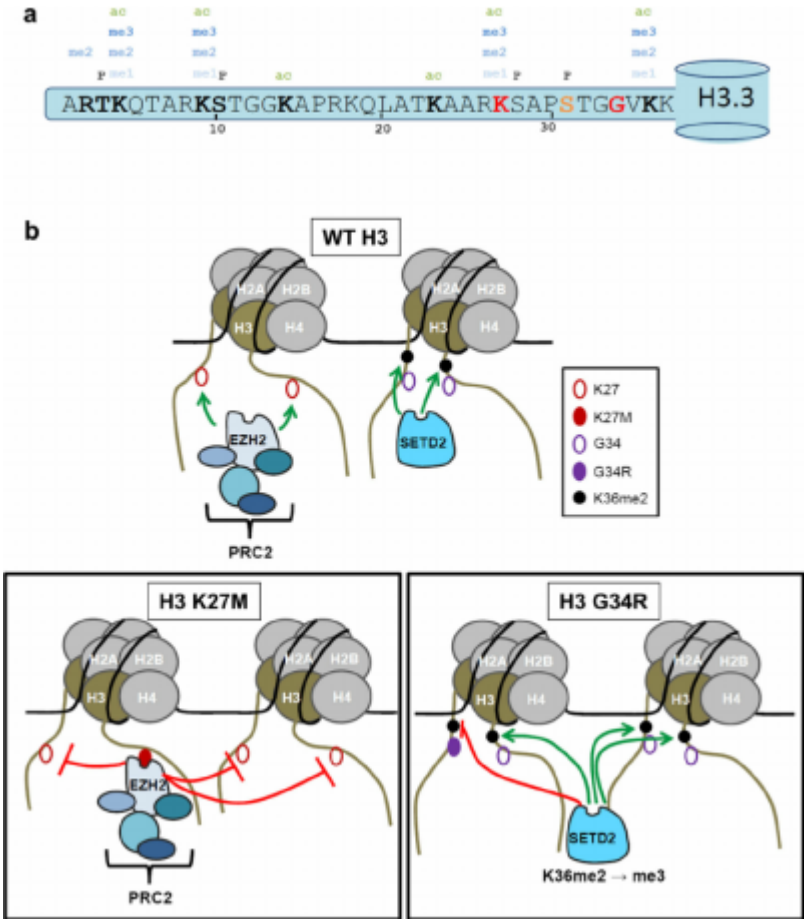
Histone H3K27 mutation



see Diffuse midline glioma H3 K27M-mutant.

Recurrent mutations in histone H3 were first reported in pediatric high grade gliomas (pHGGs). Simultaneous reports described H3K27M mutations in the majority of diffuse intrinsic pontine gliomas, as well as in thalamic gliomas [1] [2].

El Ahmadieh et al., reported two young adult patients with histone H3K27 mutation in thalamic pilocytic astrocytomas who presented to medical attention with symptomatic hydrocephalus requiring urgent intervention.

They presented the experience with this unusual tumor and recommend a treatment paradigm of maximal safe resection followed by chemotherapy and radiation.

Stereotactic biopsy may undergrade some adult thalamic pilocytic astrocytomas. Thus, they recommend that all of these tumors be evaluated for the H3 K27M mutation. Further, they believe that H3 K27M-mutant thalamic pilocytic astrocytomas require aggressive multi-modality treatment and that these treatments should be guided by the molecular findings, as opposed to the histologic ones [3].

Katz et al., set out to identify potential prognostic implications of epigenetic modification on the level of histones with focus on H3K27 trimethylation (H3K27me3). H3K27me3 was assessed by

immunohistochemistry on 232 meningiomas from 232 patients. In 194 cases, trimethylation was detected in tumor cells. In 25 cases, staining was limited to vessels while all tumor cells were negative. Finally, 13 cases yielded equivocal staining patterns. Reduced abundance of H3K27me3 in cases with staining limited to vessels was confirmed by mass spectrometry on a subset of cases. Lack of staining for H3K27me3 in all tumor cells was significantly associated with more rapid progression ($p = 0.009$). In line, H3K27me3-negative cases were associated with a DNA methylation pattern of the more aggressive types among the recently introduced DNA methylation groups. Also, NF2 and SUFU mutations were enriched among cases with complete lack of H3K27me3 staining in tumor cells ($p < 0.0001$ and $p = 0.029$, respectively). H3K27me3 staining pattern added significant prognostic insight into WHO grade II cases and in the compound subset of WHO grade I and II cases ($p = 0.04$ and $p = 0.007$, respectively). However, it did not further stratify within WHO grade III cases. Collectively, these data indicate that epigenetic modifications beyond DNA methylation are involved in the aggressiveness of meningioma. It also suggests that H3K27me3 immunohistochemistry might be a useful adjunct in meningioma diagnostics, particularly for cases with WHO grade II histology or at the borderline between WHO grade I and II [4].

After the start of the era of biopsy, Diffuse intrinsic pontine gliomas (DIPG)s bearing Histone H3K27 mutations have been reclassified into a novel entity, diffuse midline glioma, based on the presence of this molecular alteration. However, it is not well established how clinically diagnosed DIPG overlap with H3 K27-mutated diffuse midline gliomas, and whether rare long-term survivors also belong to this group [5].

References

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