Histone H3

Histone H3 Lysine 27 (H3K27): Histone H3 is a protein involved in packaging DNA in the cell nucleus. H3K27 refers to a specific amino acid, lysine, at position 27 on the histone H3 protein. Modifications to H3K27 play a crucial role in the epigenetic regulation of gene expression.

Histone H3 is a nuclear core histone protein of DNA chromatin, with an important role in chromosome condensation and cell cycle progression during mitosis and meiosis after phosphorylation of serine-10 and serine-28 residues. Phosphorylation occurs during late G2 to early prophase, while dephosphorylation occurs slowly from late anaphase to early telophase. Therefore in metaphase, histone H3 is always heavily phosphorylated and positive for PHH3, whereas interphase does not or minimally express PHH3 – a property that allows PHH3 to stain only mitotically active cells, therefore proliferation-specific.

PHH3 has been verified in multiple studies concerning various tumors (colorectal adenocarcinoma, ovarian serous adenocarcinoma, pulmonary neuroendocrine carcinoma, uterine smooth muscle tumors, astrocytomas, and meningiomas), for its sensitive and specific role as a marker of mitotic figures (MFs) and excellent correlation with outcome

Histone H3 phosphorylation on serine-10 is specific to mitosis and phosphorylated histone H3 (PHH3) proliferation markers (as counts defined per area or as indices defined per cell numbers) are increasingly being used to evaluate proliferation in various tumors.

Medical records were retrospectively reviewed for all intracranial meningioma cases which diagnosed and underwent surgery at Bezmialem Vakif University Hospital between 2012 and 2017. All World health organization grade 1 meningioma and World health organization grade 2 meningioma patients constituted the core sample for this study.

This series included 104 (69 female, 35 male) patients, with a median age of 57.3 years. The mean preoperative course was 23.0 ± 40.5 months. The most common symptom was headache (76%) and followed by seizure (24%), weakness (18%) and visual disturbances (14%). Seventy one (68.2%) patients were diagnosed as WHO grade I meningioma and 33 (31.8%) were WHO grade II, World health organization grade 3 meningiomas were excluded from study due to small number of patients. Subtypes of meningioma includes 5 angiomatous meningioma (4,8%), 6 fibroblastic meningioma (5.7%), 1 meningothelial meningioma (0,9%), 11 psammomatous meningioma (10,5%), 3 secretory meningioma (2,8%), 43 transitional meningioma (41,3%) and 33 atypical meningiomas (31,7%). There is a strong correlation with Phosphohistone H3 (PHH-3) and Ki-67 (p:0,001>) and mitosis index (p:0,001 >) although there is no correlation with STAT3 (p:0,260). There is a strong correlation with STAT-3 and Ki-67 (p:0,013), although there is no correlation with mitosis index (p:0,085) and PHH-3 (p:0,260).

In the study they also obtain same results with Ki-67 and mitotic index, although correlation with PHH-3 and STAT-3 is firstly determined and there was no statistically significant relation were observed. Depends on the STAT-3 cell proliferation feature, inactivation of these pathways may predict new chemotherapies for grade II meningiomas [1)].

Elmaci et al. from the Department of Neurosurgery, Memorial Hospital, Sisli, Istanbul, Turkey, review data on PHH3 proliferation markers in meningeal tumors. PHH3-staining highlights mitotic cells and makes easier of rapid grading by driving pathologist's attention on the most mitotically active areas. Thereby, it would function more sensitive in detecting MFs that might be otherwise overloked and more precise by reducing interobserver variability through allowing the pathologist to analyze if the stained nuclei exhibit morphologic features of mitosis [2].

References

[1]
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[2]
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