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Title: Global histone H3 lysine 4 (H3K4) dimethylation is an important prognostic factor in lung cancer

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Body: [Introduction] Epigenetic modifications may contribute to the development and progression of cancer. This study seeks to elucidate the role of global histone modifications as a clinicopathological factor in lung cancer. [Methods]A series of 92 surgical specimens from patients with lung cancer were utilized from the surgical files of Kanazawa Medical University Hospital between 2001 and 2008. The 92 tumor specimens were examined by immunohistochemistry. Dimethylated histone 3 lysine 4 (H3K4diMe), Acetylated histone 3 lysine 9 (H3K9Ac), acetylated histone 3 lysine 18 (H3K18Ac), trimethylated histone 3 lysine 27 (H3K27trime), himethylated histone 4 arginine 3 (H4R3diMe) was assessed in paraffin-embedded tumor samples. They were dichotomized into two categories as low expression and high expression. The association between staining intensity and clinicopathological factor was analyzed. [Results]Lung cancers of various histologic subtypes showed that dimethylated histone 3 lysine 4 (H3K4diMe), acetylated histone 3 lysine 9 (H3K9Ac), acetylated histone 3 lysine 18 (H3K18Ac), trimethylated histone 3 lysine 27 (H3K27trime), dimethylated histone 4 arginine 3 (H4R3diMe) were high expressed in tumor cells of 40, 10, 9, 9, 10%. Expression of dimethylated histone 3 lysine 4 (H3K4diMe) correlated positively with recouurence (p=0.039) and stage (p=0.005) and cell differentiation (p=0.002). Univariate analysis showed that high expression of dimethylated histone 3 lysine 4 (H3K4diMe) correlated with recouurenc [Conclusion]We hypothesize that expression of H3K4diMe may be considered as a significant factor for patients with lung cancer.