Evaluation of the H3K9ac immunoexpression in lip carcinogenesis


Abstract
Actinic cheilitis (AC) is a potentially malignant lesion caused by long period sun exposure. Mainly affects the lower lip and can develop into a lip squamous cell carcinoma (LSCC). Acetylation of lysine 9 in histone 3 (H3K9ac) is an epigenetic mechanism that regulates gene expression by chromatin decondensation. H3K9ac was more intense in LSCC (n=40) than AC (n=42) and LNM(n=47). No differences were observed between LSCC and AC (WHO – Severe dysplasia; Binary System – High risk). Our results suggest that H3K9ac could be a promising marker to indicate AC’s malignization.

Key words: Histones, Epigenetic process, Lip neoplasm.

Introduction
Epigenetic events are reversible and hereditary modification without genomic alteration, like H3K9ac. H3K9ac is associated with lower chromatin condensation level, causing more genes expressions and favoring mutations. H3K9ac immunohistochemical expression were described in intraoral cancer (1), which has different etiology factors from lip carcinogenesis (2). However, this marker was not assessed in lip carcinogenesis yet. This study proposes to identify H3K9ac immunohistochemical expression in lip normal mucosa (LNM), actinic cheilitis (AC), and lip squamous cell carcinoma (LSCC).

Results and Discussion
47 LNM, 42 AC, and 40 LSCC were selected. 5µm histological slices stained in hematoxylin-eosin were performed and analyzed by WHO and Binary System Classification for epithelial dysplasia and cancer differentiation. Additionally, 3µm histological slices suffered immunohistochemical reaction (anti-H3K9ac, C5B11, Cell Signaling). These slides were digitized and quantified (Aperio Technologies, Leica Biosystems), and data values were statistically analyzed.

Statistical test was made for assess H3K9ac differences among groups. H3K9ac was more observed in LSCC than AC and LNM. No differences were observed between LSCC and AC (WHO – Severe dysplasia; Binary System – High risk). These results corroborate with WHO definition about high grade epithelial dysplasia should be considered as an in situ carcinoma (not yet invasive) (2).

Conclusions
Our results suggest that H3K9ac could be a promising marker to indicate AC’s malignization. Additionally, from the epigenetic point of view, severe/high risk lip epithelial dysplasia should be considered as an early stage of squamous cell carcinoma.

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