

## Different expression patterns of carbonic anhydrase IX in oral lichen planus and leukoplakia

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### ABSTRACT

Tumor hypoxia is an important indicator of cancer prognosis. Among the different genes that are up-regulated by hypoxia is carbonic anhydrase IX, which combines carbon dioxide and water to form bicarbonate and hydrogen. Although expression of this enzyme is very low in normal tissues, carbonic anhydrase IX is overexpressed in several types of cancer. The aim of the present work was to analyze carbonic anhydrase IX expression in the two most frequent potentially malignant oral disorders: oral lichen planus and oral leukoplakia. Immunohistochemical analysis of oral lichen planus and oral leukoplakia biopsies was performed using anti-carbonic anhydrase IX antibody. Samples of normal mucosa served as controls. Statistical analysis was performed by Fischer's exact test. The enzyme was detected in the epithelium of

both lesions. The staining was more intense in the basal layer and decreased towards the surface in oral lichen planus. Conversely, the most intense reaction was observed in the superficial layers in leukoplakia, and staining intensity decreased towards the basal membrane. No carbonic anhydrase IX expression was seen in normal mucosa samples. Carbon anhydrase IX expression in lichen and leukoplakia epithelia shows that hypoxia plays a role in the pathogenesis of both lesions. The different distribution patterns provides further evidence of the different biological behavior of these two entities, which under certain circumstances can have similar clinical and histological features.

**Key words:** Carbonic Anhydrase IX; Oral Lichen Planus; Oral Leukoplakia.

## Diferentes patrones de expresión de la anhidrasa carbónica IX en liquen plano bucal y leucoplasia

### RESUMEN

La hipoxia tumoral es un importante indicador de pronóstico en cáncer. Entre los distintos genes que son activados por hipoxia, uno de los principales es la anhidrasa carbónica IX (CAIX), que combina  $CO_2$  con  $H_2O$  para sintetizar  $HCO_3^-$  y  $H^+$ . Aunque la expresión de esta enzima es muy baja en tejidos normales, se sobreexpresa en varios tipos de cáncer. La finalidad del presente trabajo fue analizar la expresión de CAIX en las dos lesiones orales potencialmente malignas más frecuentes: el liquen plano y la leucoplasia. Se utilizó una técnica inmunohistoquímica con un anticuerpo específico contra CAIX, en biopsias de liquen plano oral y leucoplasia oral. Se utilizaron mucosas normales como controles. Se realizaron análisis estadísticos utilizando test exacto de Fischer. La identificación

de la enzima fue positiva en el epitelio de ambas lesiones. En los líquenes la reacción es más intensa en los estratos basales, disminuyendo hacia la superficie. Inversamente, las leucoplasias mostraron marcación más intensa en estratos superficiales, con disminución hacia la membrana basal. Las mucosas normales resultaron negativas. La expresión de CAIX en el epitelio de líquenes y leucoplasias indica que la hipoxia juega algún papel en la patogenia de ambas lesiones. El diferente patrón de distribución es una evidencia más del diferente comportamiento biológico de dos entidades las cuales en ciertas circunstancias pueden manifestar cuadros clínicos e histológicos semejantes.

**Palabras clave:** Anhidrasa Carbónica IX; Liquen Plano Oral; Leucoplasia Oral.

### INTRODUCTION

Tumor hypoxia is an important indicator of cancer prognosis, since it is associated with aggressive growth, metastasis and poor response to treatment<sup>1</sup>. Genes that are up-regulated by microenvironmental hypoxia through activation of Hypoxia Inducible

Factor-1 (HIF-1) include glucose transporters, glycolytic enzymes, and angiogenic growth factors<sup>2</sup>. Carbonic anhydrases (CAs), a family of metalloenzymes that require  $Zn^{2+}$  as a cofactor, are one of the most important groups. Sixteen isozymes that differ in their subcellular localization, catalytic activity

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