Energy metabolic profile in oral potentially malignant disorders and oral squamous cell carcinoma

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Abstract

We hypothesized that cell energy metabolic profiles correlate with normal, dysplastic, and tumor cell/tissue statuses and may be indicators of aggressiveness in oral squamous cell carcinoma (OSCC) cells.The energy-related proteins that were differentially expressed in human OSCC fragments (n=3) and their adjacent epithelial tissue (TAE) were verified using mass spectrometry. Immunohistochemistry for 4-hydroxynonenal (4-HNE) was performed to evaluate the oxidative stress patternsin OSCC (n=10), epithelial dysplasia (n=9), and normal epithelial (n=4) biopsies. The metabolic modulation of OSCC aggressiveness was investigated in human OSCC cell lines with different levels of epithelial–mesenchymal transition proteins. All OSCC fragments exhibited an increase in glycolysis-related proteins and a decrease in mitochondrial activity compared to the TAE region ($p<0.05$), probably due to the downregulation of pyruvate dehydrogenase and antioxidant proteins. Additionally, the OSCC cell line with a mesenchymal profile (SCC25) had a lower mitochondrial mass and membrane potential and generated lower levels of reactive oxygen and nitrogen species than the TAE region. When we analyzed 4-HNE, the reactive species levels were increased in the epithelial regions of OSCC and potentially malignant lesions. A decrease in the levels of 4-HNE/reactive species was observed in the connective tissue underlying the dysplastic regions and the OSCC invasion zone.Thus, aggressive OSCC is associated with high glycolytic and oxidative metabolism and low mitochondrial and antioxidant activities, which vary according to the differentiation level of the tumor cells and the stage of carcinogenesis.

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