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## **Immunohistochemical expression of oxidative stress markers Keap1, Nrf2 in oral squamous cell carcinoma in relation to (angiogenesis, invasion, and metastasis) assessed by VEGF-C and Integrin- $\beta$ 1 in comparison to the normal oral mucosa**

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Oxidative stress has been reported to play an important role and implicated in etiology of various kinds of malignancies and benefit cells through initiation, survival, and progression. Keap1, Nrf2 were considered as a clue on the balance between oxidation and antioxidants mechanism inside normal and malignant cells, their clinical significance and role in biological behavior of oral squamous cell carcinoma has to be elucidated, in addition to their relation to VEGF-C and Integrin- $\beta$ 1 as a markers of angiogenesis, invasion, and metastasis has to be clarified. A total of forty formalin fixed paraffin-embedded blocks of oral squamous cell carcinoma and fifteen cases of normal oral mucosa were studied. An immunohistochemical staining was performed using anti Keap1, Nrf2, VEGF-C and integrin- $\beta$ 1 antibodies. All the tested tissue markers were overexpressed in tumor cells comparing to normal corresponding tissue. VEGF-C was in direct relation to tumor size. With the tumor stage, only integrin- $\beta$ 1 has a statistically direct relationship. All markers had no relations either to the degree of differentiation, nor inflammatory reaction, with the exception of Nrf2 marker, however, it showed a statistically significant moderate positive direct linear correlation with degree of inflammatory reaction. Overexpression of oxidative stress Keap1, Nrf2, proteins in oral squamous cell carcinoma enhances cytoprotective effects on cancer cells and may contribute to diverse cellular functions in conjunction with the expression of VEGF-C and integrin- $\beta$ 1 proteins in cancer cells, such as differentiation, proliferation, inflammation, and metastasis.

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