

**No: OP/G-B32**

## **RANKL, RANK and OPG expression in Human Oral Premalignant and Malignant Epithelial Lesions**

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### **Abstract**

**Purpose:** The purpose of the present study is to investigate the immunohistochemical of NF- $\kappa$ B (RANK), NF- $\kappa$ B ligand (RANKL) and osteoprotegerin (OPG) in human oral premalignant and malignant epithelial lesions.

**Materials and methods:** Immunohistochemical analysis of RANK, RANKL and OPG protein expression was performed in human oral premalignant and malignant epithelial lesions. Surgical human oral specimens with the following histological diagnoses were collected: mild (n=10), moderate and severe (n=10) dysplasia; submucous fibrosis (n=10); verrucous hyperplasia (n=10), verrucous carcinoma (n=10); squamous cell carcinoma (well-differentiated, n=10; moderate-differentiated and poor-differentiated, n=10); normal oral mucosa (n=5).

**Results:** Strong cytoplasmic staining of RANKL proteins is detected in cancer cells of verrucous hyperplasia, verrucous carcinoma and SCCs. The same protein is identified in cytoplasm of mild, moderate and severe dysplasia; and submucous fibrosis. Strong cytoplasmic staining of RANKL is confined to basal layer for all normal mucosa. A

similar staining pattern is noted for RANK protein in all premalignant and malignant lesions. An absence of staining of RANK protein is noted for all normal tissues. Weak to negative cytoplasmic stained OPG protein is present in all premalignant and malignant lesions, but is absent in all normal tissues.

***Conclusions:*** The results of this study demonstrate the association between RANK, RANKL and OPG expression in human oral premalignant and malignant epithelial lesions, and suggest that osseous destruction by SCC in the human oral cavity appears to be mediated by the cancer cell itself through the activation of osteoclasts via a RANKL/RANK/OPG pathway.