# Co-expression of CD44+/RANKL+ tumor cells in the carcinogenesis of oral squamous cell carcinoma



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Abstrak

Receptor activator of nuclear factor-kappa (RANK)/receptor activator of nuclear factor-kappa B ligand (RANKL) signaling helps putative cancer stem cells (CSC) to maintain their stemness. Expression of CD44 and RANKL was analyzed in oral squamous cell carcinoma specimen (n = 191). Moreover, RANKL expression was measured in cancer cell lines (BICR3, BICR56) by immunohistochemistry and western blot analysis. Scanned images were digitally analyzed using ImageJ and the immunomembrane plug-in. CD44 and RANKL expression on protein level was correlated with clinical characteristics and impact on survival. RANKL was co-labeled with CD44 in immunohistochemical and immunofluorescence double labeling experiments. Although high CD44+/RANKL+ co-expression was significantly associated with clinicopathological factors and worse survival, multivariate analysis did not demonstrate high CD44+/RANKL+ co-expression as independent prognostic factor. Immunohistochemical and immunofluorescence double labeling experiments revealed RANKL expression by CD44+ cancer cells. RANKL specificity was confirmed by western blot analysis. For the first time, this study provides evidence that RANKL expression in OSCC might be associated with disease recurrence and a cell compartment measured by CD44+/RANKL+ co-expression within the mucosal epithelial basal layer cells.