

Differential Expression of VEGF and PAI-1 in Oral Squamous Cell Carcinoma.

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Abstract:

Vascular Endothelial Factor [VEGF] is an endothelial cell-specific mitogen that regulates most steps of the angiogenic process, including endothelial cell degradation of extracellular matrix (ECM), migration, proliferation, and tube formation. In keeping with its ability to induce ECM degradation, VEGF increases the expression and activity of plasminogen activators, urokinase type plasminogen activator (uPA) and tissue type plasminogen activator (tPA). Both proteases are specifically inhibited by plasminogen activator inhibitor type 1 (PAI-1), the expression of which is also up regulated by VEGF. Specific Aims: To examine the differences between VEGF and PAI-1 expression in oral squamous cell carcinoma [SCCs] and normal human oral keratinocytes [NHOK]. Experimental Design: 1- Cell lines and culture conditions: a- A total of three human oral cancer cell lines [Cal33, SCC-4 & SCC-9] and NHOK isolated from different sites of oral mucosa [Tongue, Gingiva, & Palate]. b- Cells were grown to 80% confluence, and subjected to different conditions, Normoxia [20% O₂] and Hypoxia [2% O₂]. 2- VEGF & PAI-1 were examined on both translation and transcription levels using the following: a- Northern Blot Analysis, b- Enzyme-Linked immunoAbsorbant assay [ELIZA], c- Zymography of PAI-1 (Reverse fibrin overlay), d- Western Blot Analysis and e- Immunocytochemistry. Results: Hypoxia upregulated VEGF and PAI-1 expression on both normal and oral cancer cell lines, with a statistically significant difference between normal and oral cancer cell lines. Pattern of hypoxia induced VEGF mRNA level tightly followed the PAI-1 mRNA expression in the cell lines tested. From the above results, we conclude that oral Squamous cell carcinoma express VEGF and PAI-1 more than NHOK that are upregulated by hypoxia. VEGF and PAI-1 can play a role in oral cancer angiogenesis, progression and invasion.

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