Deregulated expression of key components of phosphoinositide 3 kinase pathway in oral squamous cell carcinoma

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Abstract

Oral squamous cell carcinoma (OSCC) is sixth common cancer in males globally. Deregulation of phosphatidylinositol-3-kinase (PI3K) pathway leads to various intracellular responses such as proliferation, survival, and inhibition of apoptosis. We evaluated the expression of key components of PI3K pathway in OSCC patients. RT-PCR and qRT-PCR was used assess the expression of different AKT isoforms, PTEN, TSC1 and TSC2 in tumor and normal tissues. The expression of various components of PI3K pathway e.g. Ser473pAKT, pan-AKT, PTEN and Ser2448mTOR and mTOR was evaluated by western blot assay. Effect of selected PI3K inhibitors on OSCC cells (SCC-4, SCC-9 and SCC-25) was also studied. Approximately 1.4-fold higher expression of AKT1 and downregulation of AKT2 and AKT3 mRNA was observed in tumor tissue sections of patients as compared to controls. PTEN, TSC1 and TSC2 mRNA was found to be marginally decreases in tumor than the normal area. Significantly strong immunostaining of ser473p-AKT in comparison to AKT1 was documented in all paraffin fixed oral cancer tissues. Additionally, a strong positive correlation between the immunohistochemical expression of AKT-1 and ser473p-AKT in the paraffin sections of oral cancer tissues was observed (r= 0.7504; p≤0.0001). Aberrant expression of key components of PI3K pathway was also found in OSCC cells that were reversed with the treatment of its inhibitors. Overall, our study suggests that PI3K pathway is deregulated OSCC patients and OSCC cell lines, with AKT1 being the predominantly expressed isoform. PI3K inhibitors restored such aberrations in OSCC cell lines.

Keywords

PI3K, AKT1, mTOR, mRNA, oral cancer.

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References