Background: Basal cell carcinoma (BCC) develops predominantly in sun-exposed skin in fair-skinned individuals prone to sunburn. BCC typically occurs in adults. High exposure to ultraviolet (UV) radiation increases rate of developing BCC, a slowly growing tumor that occurs in hair-growing squamous epithelium and rarely metastasizes. In genetic studies, BCC patients have cell-cycle abnormalities of different parts of the signaling pathway. Retinoblastoma regulatory pathway is important in cell cycle arrest. In this pathway, p16INK4a, an inhibitor of Rb pathway, binds to CDK4 and CDK6 competitively with cyclin D1 to prevent phosphorylation of tumor suppressor pRB gene. Alteration of this pathway contributes to development of human cancers and also is effective in skin cancers. In this study, we analyzed mRNA expression using in situ RT-PCR and the role of immunohistochemical expression of p16INK4a in BCC. Methods: Expression of p16 in ten samples of Iranian paraffin-embedded skin BCC were studied using in situ RT-PCR and immunohistochemistry on p16INK4a gene. Results: Nuclear and cytoplasmic staining intensity of samples within tumor cells and normal skin tissue illustrates different mRNA and protein expression of p16 gene. mRNA of p16 gene and the expressed protein induce cell cycle proliferation and involve both tumor tissue as well as normal skin tissue. However, in this study it was found that there is significant protein and mRNA expression in BCC cells when compared to normal skin tissue (p <0.05). Conclusions: p16 gene is involved in the pathogenesis of human skin BCC in view of increased p16 mRNA and expressed protein within tumor cells.

**Keyword:** Basal cell carcinoma; Immunohistochemistry; p16; Retinoblastoma pathway; RT in situ PCR; Skin cancer.