

EFFECTS OF TUMOR NECROSIS FACTOR (TNF) TREATMENT ON HPV 16 E7-EXPRESSING KERATINOCYTES GENE EXPRESSION PROFILE

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Keratinocytes are the natural target cells for infection by human papillomaviruses (HPVs). The high-risk HPVs cause lesions that can progress to carcinomas. TNF is a pro-inflammatory cytokine produced by cells in response to a viral infection which has a potent cytostatic effect on normal keratinocytes. We have shown that expression of HPV 16 or 18 E7 oncogene is sufficient to overcome TNF antiproliferative effect in monolayer and organotypic cell cultures. Furthermore, we observed that pRb degradation induced by E7 is essential to mediate TNF-resistance. In this study we compared the effects of TNF between normal and HPV16 E7 expressing keratinocytes. Amplified RNA from monolayer cultures were analyzed by cDNA microarray hybridization using glass arrays with 4800 human genes with known function. Our preliminary data shows that a number of genes involved in induction of cell proliferation and regulation of differentiation were differentially regulated between TNF-resistant E7-expressing cells and normal cells. The identification of specific changes in gene expression in E7 harboring cells may contribute to understand the mechanisms of E7-mediated TNF-resistance and have other insights of its oncogenic potential.

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