Analysis of the differential expression of genes involved in process related to oral carcinogenesis in an in vitro tumor microenviroment

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Resume

Objetives. To compare the differential expression of genes that contribute to oral carcinogenesis and that are associated with stress responses in normoxia and hypoxia, both in the parental HaCaT cell line, and in the HaCaT cell line transduced with the HPV-18 E5, E6 and E7 viral oncogenes (HaCaT E5/E6/E7-18).

Methods. Human keratinocytes that were spontaneously immortalized (HaCaT) and also the same HaCaT cell line but transduced with HPV-18 (E5/E6/E7) oncogenes, were used. Both cell lines were exposed to a hypoxic microenvironment, by inducing hypoxia with the coverslip method. First, protein extractions were performed on both lines, which were quantified using the Bradford colorimetric method. Subsequently, two arrays of commercial proteins were made; on the one hand, proteins associated with carcinogenesis and, on the other, proteins associated with cellular stress. Finally, protein levels were quantified using ImageQuant TL software (GE Healthcare).

Results. Significant differences were observed in the expression levels of proteins related to carcinogenesis between the parental HaCaT cell line and the HaCaT E5/E6/E7-18 cell line, under normoxia and hypoxia conditions. Higher expression of the protumoral proteins galectin-3, phospho-38α, phospho-JNKpan, thioredoxin-1, HSP-70, HIF-1α and SOD2 was observed in HaCaT E5/E6/E7-18 in both conditions. In addition, a higher expression of BCL-x and CapG was observed in HaCaT cells in normoxia, compared to the HaCaT E5/E6/E7-18 line in normoxia.

Conclusions. The results suggest that the presence of the HPV-18 (E5/E6/E7) oncogenes, together with the induction of hypoxia, influence the expression of proteins that are involved in carcinogenesis and cellular stress.

Keywords. Oncogenes, hypoxia, HPV-18, stress.

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