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Meeting abstract

Role of HPV18 E6 in PKB signal transduction pathways

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Background

The etiological role of Human Papillomavirus (HPV) in cervical cancer development has been clearly demonstrated, it is known that only a minority of cervical lesions infected with high risk HPVs evolve to higher grade lesions or cervical cancer. It is thought that intratype HPV variations may play an important role in differences in viral biological behaviour. It has been recently reported that E6 protein of high risk HPVs degrades proteins such as p53, Bak, Myc and hDlg which are involved in cellular processes such as proliferation, apoptosis and maintenance of cyto-architecture possibly by the PKB pathway. The objective of this study was to determine the differential contribution of E6 from variants of HPV18 in cell proliferation through the Akt/PKB pathway.

Materials and methods

C33, cervical cancer cell line HPV negative (mutated in p53), and MCF-7 breast cancer cell line (wt p53), were transfected with different E6 genes from HPV18 – Asian Amerindian, -European, and -African variants. Protein levels of p53, hDlg, PI3K, PTEN, PKB and activated forms were determined by Western Blot. Proliferation was analyzed by methylene blue and flow cytometry assay. Immunohistochemistry was performed in cell lines and cervical cancer tumor biopsies.

Results

Proliferation was significantly diminished in cells transfected with African E6 in relation to -European or -Asian Amerindian clones. This fact is correlated to an increase in hDlg protein levels in cell lines harboring the E6 African variant; as well as an increase in PI3K and PKB activated forms in cells with the E6 European and -Asian Amerindian genes. hDlg was found abnormally localized in these cell lines.

Conclusion

Cell proliferation is induced by E6 of HPV18 independent of p53, this effect may be probably related to its effect over certain elements of the akt/PKB pathway. This work could help us to identify possible E6 targets in signal transduction and cell architecture, as well as biological differences between HPV18 variants.