

CELLULAR TARGETS OF HPV16 E6E7 ONCOPROTEINS IN CERVICAL CANCER

Fernanda Batista Andrade*, Edécio Armbruster-Moraes, Aurora M. Cianciarullo

Genetics Laboratory, Butantan Institute, São Paulo, Brazil.

Most cervical carcinomas express high-risk Human Papillomavirus (HPV) E6 and E7 proteins, which neutralize cellular tumor suppressor function. The E6 oncoprotein encoded by the virus is multifunctional presenting numerous cellular targets; however, it is not clear if all these activities are related to the cellular malignancy. In this study we evaluate the distribution in HPV-transformed and non-transformed mammalian cells of: E6 and E7 oncoproteins, mitochondria, transferrin receptors (TfR), transferrin (Tf) and ferritin (Fe) for the iron endocytic pathway in human and animal cells, as alternative pathway for HPV infection. HPV-negative cell lines were transfected with the pLXSN vectors, containing the complete sequence of E6 and E7 gene. Cells transformed by HPV were used as positive controls. Immunofluorescence assays were analyzed by laser scanning confocal microscopy (LSCM). Western blotting as control of proteins expression was used. The antibodies recognized the E6 and E7 oncoproteins in HPV-transformed cells and in pLXSN vector transfected cells. TfR were detected in abundance at the plasma membrane of cells, as well as the Fe was labeled in the cytoplasm, nucleus and mitochondria. The great amount of iron suggests a participation of this element in the HPV cells transformation, keeping the mitochondrial cytochrome *c* levels. Co-localizations of E6 into mitochondria were detected in HPV-transformed cells, suggesting its involvement in the process of apoptosis inhibition, which places E6 as a promising therapeutic target. Our results are in accordance to the findings of that E6 proteins degrade Bak, an apoptogenic mitochondrial factor that undergoes a conformational change, leading to the pore formation in the mitochondrial membrane and protect keratinocytes from apoptosis.

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