
P-39; p63 VALUE IN CERVICAL BIOPSY TISSUES

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Background: The relationship between HPV infections and disease of the human uterine cervix is well established, ranging from CIN (cervical intra-epithelial neoplasia) to SCC (squamous cell carcinoma). Several studies showed correlation between papillomavirus life cycle and differentiation program of infected host cell, in order to produce mature virions in squamous, differentiated cells. The majority of cervical HPV infections are transient. By contrast, persistent HPV infections are much more likely to progress to pre-malignant and malignant cervical lesions than transient productive infections. Under these conditions, it is believed that viral persistence only occurs upon targeted infections of specific cervical cells such as stem cells. Extension of stem cells theory to solid tumor offers support for new hypothesis in tumorigenesis.

Objectives: In order to understand the mechanism that governs balance between epithelial regeneration and transformation we investigated p63 expression, a tumor-suppressive protein considered a marker of keratinocyte stem cell.

Materials and Methods: p63 expression was evaluated in immunohistochemistry and RT-PCR using HOPE-fixed, paraffin-embedded biopsies from 47 women (33–54 years old) presenting abnormal cytology, with or without positive test for HPV (Linear Array Roche). On the other hand we investigated the association of EP-CAM immunohistochemical expression with differentiation-related and/or neoplastic changes in cervical epithelium.

Results: p63 expression was identified in basal/subcolumnar cells. Metaplastic (squamous or mucinous) epithelia, either alone or in conjunction with hyperplasia or carcinoma, exhibited the most intense staining, primarily in basal or subcolumnar cells. In dysplasia, exceeded p63 immunostaining was noted in 1/3 lower epithelial layer. RT-PCT revealed a correlation between higher p63 mRNA levels and the severity of lesions.

Conclusions: These results were also sustained by balance between cytokeratins detected by immunohistochemistry. HR HPV transformed cells maintain stem cell characteristics in advanced disease stage.