Abstract:

The role of HPV in the carcinogenesis of intraepithelial and invasive anogenital lesions is currently well established. E6 and E7 oncoproteins of high-risk HPV genotypes are known to inactivate p53 and pRb pathways. Several studies have described an increased prevalence and recurrence of both cervical HPV infection and invasive cervical cancer among HIV-1 positive women compared to HIV-1 negative cases. For these reasons, cervical cancer is considered an AIDS-defining neoplasm. Unlike other AIDS-associated neoplasms, the occurrence of cervical cancer is independent of immune suppression. HIV-1 infection in patients with high grade precancerous lesions and invasive cervical cancers results in a therapy refractory and more aggressive disease phenotype, which is not yet well understood at the molecular level. An upregulation of HPV E6 and E7 gene expressions by HIV-1 proteins such as Tat has been documented by some authors. However, the role of HIV-1 in cervical carcinomas is still unclear. It is already known that HIV-1 Tat protein is able to influence cell cycle progression. Altogether, these facts led us to investigate the effects of Tat on the expression of cell cycle regulator genes. After transfection of HeLa cells with Tat, we analyzed the expression of cell cycle regulators from these cells by IHC and Real-time PCR. A significant reduction in the expression of cell cycle inhibitors of transcription and an increase in the levels of proliferation markers were observed. These results suggest that HIV-1 may enhance cervical carcinogenesis by promoting cell cycle progression. We also found that this HIV-1 Tat-induced cell proliferation was not dependent on the E2F family of transcription factors, and therefore postulate that Sp factors may be involved.