**Abstract**

**Objective:** To examine the association between the presence of HPV specific T cell response in relation to HLA class I, HLA-G and IL-10 expression in the tumor cells of cervical cancer patients. **Materials and methods:** Lymphocytes were isolated from 18 cervical cancer patients and stimulated with autologous HPV16 E7-pulsed monocyte-derived dendritic cells or directly with synthetic peptides: E751-70, E765-84, and E779-98. The cells were stained for CD4, CD69, intracellular IFN-γ and IL-4 cytokines and analyzed by flow cytometry. HLA-I, HLA-G and IL-10 expression on tumor cells was analyzed by immunohistochemistry. **Results:** HLA class I expression was completely lost in 11/18 and downregulated in 4/18 of patients. HLA G expression was observed in 4/18 of patients and IL-10 expression was observed in 6/17 of patients. An inverse association between IL-10 expression and a lack of HPV-specific immune response was observed (P = 0.041). No clear associations between HLA class I or HLA-G expression and specific immune response were observed. **Conclusions:** Our results underline the importance of other immune factors, like IL-10 expression, that could influence the antitumoral response. These results could have important implications during development of new therapeutic strategies like immunotherapy.

**Key words:** T-lymphocytes, helper-inducer; HLA antigens; tumor escape; uterine cervical neoplasms, papilloma
IL-10 expression is associated with lack of HPV-16 E7 specific Th1 response in cervical cancer patients

IL-10 y la falta de una respuesta inmune específica (P=0.041). Ninguna asociación fue observada entre la expresión de HLA clase I o la expresión de HLA-G con la respuesta inmune. **Conclusiones:** Nuestros resultados subrayan la importancia de otros factores inmunes, como la expresión de IL-10, que podrían influir en la respuesta antitumoral. Estos resultados pueden tener implicaciones importantes durante el desarrollo de nuevas estrategias inmunoterapéuticas.

**Palabras clave:** linfocitos T colaboradores-inductores; antígenos HLA; escape de tumor; neoplasias del cuello uterino, papiloma.

**Introduction**

Cervical cancer is the second most common cause of death by cancer in women worldwide. Human Papillomavirus (HPV) infection is considered a major cause of cervical cancer and is detected in 99.7% of cases (1,2). Among high-risk HPV types, HPV 16 is the most prevalent accounting for approximately 50% of all cervical cancers (2,3). HPV-16 E6 and E7 genes are frequently coexpressed in tumor cells and their oncogenic effect is mediated by the binding of these viral oncoproteins to the products of tumor suppressor genes p53 and pRb respectively causing deregulation of the cell cycle (4,5). The viral transcripts of these proteins have been the most abundant found in HPV-16 positive cervical cancer biopsies to date; therefore, these oncoproteins are attractive targets for T cell-mediated immunotherapy (4,6).

Although the infection with high risk HPV (HR-HPV) is an important risk factor in cervical cancer etiopathogenesis, there is increasing evidence that the immune system plays a pivotal role in determining the outcome of HPV infections (7). It has been shown that immunosuppressed individuals are more likely to have persistent HPV infections and to develop cervical intraepithelial HPV-associated neoplasia lesions (8-10). Thus, the ability to avoid immune attack is also linked to the transforming potential of HPV and the rapid progression of human cancer (7).

Lymphoproliferative responses to specific HPV16 E6 and E7 peptides appear to be associated with the clearance of HPV infection and with the regression of cervical lesions (11-13). However, the infection of cervical epithelia by HPV is not always associated with a strong local inflammatory reaction (14) and cervical cancer may be the final stage of a persistent oncogenic HPV infection during which the host’s immune system fails to eliminate the virus (15,16).

There are several mechanisms that could explain the complex cancer–host immune interactions and the immune escape of the cancer cells in the tumor milieu. One of the major mechanisms used by tumor to escape immunosurveillance is the MHC class I molecules downregulation. In cervical cancer, a minimum of 73% loss HLA class I is estimated (17-20). It has also been reported that certain tumor cells may secrete immunosuppressive factors like IL-10 and TGF-B, which might help to downregulate tumor-specific immune responses in the microenvironment of the tumor (21). Moreover, it has been also hypothesized that HLA-G expression in cancer cells plays a role in the evasion of immunosurveillance mediated by host’s T-lymphocytes and NK cells (22,23).

To comprehend the contribution of these mechanisms to the escape of tumor cells from the actions of HPV-specific T cells, we examined the association between the presence of HPV specific T cell response in relation to HLA class I, HLA G and IL-10 expression at the tumor cell surface.

**Materials and methods**

**Patients**

Eighteen HPV 16 positive patients with invasive cervical cancer staged II A to IIIB according to FIGO (International Federation of Gynecologists and Obstetricians), being treated as outpatients at the gynecological clinic of the National Cancer Institute, in Bogotá (Colombia), were enrolled in the study. Patients were not included if they had undergone any treatment before radiotherapy (RT).