Functional role of human leukocyte antigen-G up-regulation in renal cell carcinoma.

Abstract:

The nonclassical HLA-G molecule exhibits a limited tissue distribution and exerts multiple immune regulatory functions. Recent studies indicate that HLA-G expression plays a key role in the induction of immune tolerance and may represent a novel immune escape mechanism of tumor cells. Despite a high frequency of tumor-infiltrating T lymphocytes in renal cell carcinoma (RCC) lesions, outgrowth of tumor cells occurs that might be attributable to abrogation-efficient antitumor responses. To delineate the potential role of HLA-G in RCC immunology, the HLA-G expression pattern and its functional consequences on immune responses were analyzed in cell lines and lesions derived from primary RCC lesions. A heterogeneous constitutive and IFN-gamma-inducible HLA-G mRNA and protein expression was found in 12.5% of RCC cell lines but not in autologous normal kidney cells. Western blot analysis of 37 primary RCC lesions revealed HLA-G protein expression in 27% of RCC lesions. Functional studies performed with alloreactivenatural and lymphokine-activated killer cells as well as antigen-specific CD8(+) T-cell populations demonstrated that HLA-G expression inhibits lysis of RCC cells by these different immune effector cells, whereas HLA-G(-) normal kidney cells were recognized. Furthermore, the HLA-G-mediated counteraction of immune response could be restored by antibody blocking...
experiments. Thus, aberrant HLA-G expression is found at a relatively high frequency in RCC and might participate in evasion of these tumor cells from immunosurveillance.