Diverse CD8+ T-cell responses to renal cell carcinoma antigens in patients treated with an autologous granulocyte-macrophage colony-stimulating factor gene-transduced renal tumor cell vaccine.

Abstract:
A phase I clinical trial with granulocyte-macrophage colony-stimulating factor tumor cell vaccines in patients with metastatic renal cell carcinoma (RCC) showed immune cell infiltration at vaccine sites and delayed-type hypersensitivity (DTH) responses to autologous tumor cells indicative of T-cell immunity. To further characterize RCC T-cell responses and identify relevant RCC-associated antigens, we did a detailed analysis of CD8+ T-cell responses in two vaccinated RCC patients who generated the greatest magnitude of DTH response and also displayed a strong clinical response to vaccination (>90% reduction in metastatic tumor volume). Three separate CD8+ T-cell lines (and subsequent derived clones) derived from patient 24 recognized distinct RCC-associated antigens. One recognized a shared HLA-A*0201-restricted antigen expressed by both renal cancer cells and normal kidney cells. This recognition pattern correlated with a positive DTH test to normal kidney cells despite no evidence of impairment of renal function by the patient's remaining kidney after vaccination. A second line recognized a shared HLA-C7-restricted antigen that was IFN-gamma inducible. A third
line recognized a unique HLA-A*0101-restricted RCC antigen derived from a mutated KIAA1440 gene specific to the tumor. In addition, two independent CTL lines and three clones were also generated from patient 26 and they recognized autologous tumor cells restricted through HLA-A*0205, HLA-A/B/C, and HLA-B/C. These results show that paracrine granulocyte-macrophage colony-stimulating factor tumor vaccines may generate a diverse repertoire of tumor-reactive CD8+ T-cell responses and emphasize the importance of polyvalency in the design of cancer immunotherapies.