Abstract:
Murine models for immune-mediated tumor regression have defined an essential role for CD4+ T helper (Th) cells, but the contribution of these cells to antitumoral immune responses in humans remains poorly defined. Here, we investigated the Th cell response against the autologous tumor in a patient with metastasized renal cell carcinoma (RCC) exhibiting objective clinical response to immunotherapy. Peripheral blood T cells of the patient were repeatedly stimulated in vitro using either autologous IFNγ-treated whole tumor cells or Epstein-Barr virus-immortalized B cells (EBV-B) pulsed with tumor cell lysate. CD4+ T-cell clones recognizing autologous tumor cells but not EBV-B cells were efficiently reactivated and expanded with both types of stimulator cells, establishing the latter as potentially useful for isolating CD4+ T cells reactive against MHC class II-negative tumors. Two T-cell clones from both stimulation protocol were further characterized. The restricting MHC class II molecules were defined by using allogeneic EBV-B cells pulsed with tumor lysate, and the expression pattern of the antigens was examined by analyzing lysates from normal kidney cells, allogeneic RCCs as well as tumors of different histologic origin. Furthermore, the subcellular localization of the antigens recognized by the T-cell clones was examined by fractionating the tumor lysate, and the Th phenotype was determined by assessing the cytokines released after T cell activation. These experiments
show that a dual Th1/Th2, MHC class II-restricted T-helper-cell response against diverse shared tumor antigens has been elicited in this patient.