Cancer Immunity, Vol. 3 Suppl. 1, p. 14 (6 February 2003)

Monitoring of immune responses against NY-ESO-1 in cancer patients

Elke Jäger

II. Medizinische Klinik, Krankenhaus Nordwest, Frankfurt, Germany

Abstract

NY-ESO-1 belongs to the group of 'Cancer-Testis' antigens, which are expressed in different types of cancer and normal germ line tissues. Compared to other cancer antigens, NY-ESO-1 is one of the most immunogenic antigens known to date, inducing spontaneous humoral and cellular immune responses in a large proportion of patients with NY-ESO-1+ malignancies. In collaboration with Elisabeth Stockert, Sacha Gnjatic and colleagues at the Ludwig Institute for Cancer Research, New York, we established standardized methods to monitor spontaneous and vaccine-induced humoral and cellular NY-ESO-1-specific immune reactions in cancer patients.

NY-ESO-1 serum antibody is detected by Western blot and ELISA assays in approximately 50% of patients with advanced NY-ESO-1+ cancers. Serum antibody titers correlate with the clinical development of disease. Increasing titers are associated with disease progression, and decreases with tumor regression observed after surgery or chemo-immunotherapy. Correlating with high NY-ESO-1 serum antibody titers, NY-ESO-1 antibody was detected in patients' urine by Western blot analysis.

The analysis of a larger series of patients with and without spontaneous NY-ESO-1 serum antibody showed that detectable NY-ESO-1 serum antibody is closely associated with measurable CD4+ and CD8+ T-cell responses. Based on these, a number of MHC class I and class II restricted peptide epitopes were identified that are now being used as targets for the monitoring of spontaneous or vaccine-induced NY-ESO-1-specific immune responses. Complementary methods for the assessment of NY-ESO-1-specific cellular immune responses have been standardized for the evaluation of clinical NY-ESO-1 vaccine trials. ELISPOT and tetramer assays have shown comparable results and sensitivity for the quantification of NY-ESO-1-specific CD4+ or CD8+ T lymphocytes. Cytotoxicity assays, even though considered less sensitive, have confirmed the lytic function of ELISPOT and tetramer+ effector cells against NY-ESO-1 peptide-loaded antigen presenting cells and NY-ESO-1+ tumor cell lines.

Clinical vaccine trials have been initiated to explore the immunogenicity of different NY-ESO-1 peptides or vaccine constructs. HLA-A2-restricted NY-ESO-1 peptides administered as weekly intradermal injections have induced strong peptide-specific CD8+ T-cell responses in the majority NY-ESO-1-naive patients. The onset and intensity of delayed-type hypersensitivity (DTH) reactions at the sites of peptide inoculation during the course of vaccination were found to reflect NY-ESO-1-specific CD8+ T-cell responses measurable in the peripheral blood. Modified peptide vaccine schedules and different NY-ESO-1 viral constructs are currently being evaluated for their immunological and clinical effects. The recent identification of new NY-ESO-1 peptide epitopes presented by HLA-B35 and HLA-B51 will help to expand the patient population eligible for NY-ESO-1-specific immunotherapy.