Abstract

Since the discovery of NY-ESO-1 by Yao Chen, Lloyd Old and their group in 1997 through the SEREX technology, NY-ESO-1 has evolved as one of the most immunogenic human cancer antigens known to date. NY-ESO-1 belongs to the Cancer Testis (CT) class of antigens, which is typically expressed in many types of cancers but not in normal tissues except in germ cells. NY-ESO-1 is a member of a family of related cancer antigens, some of which were discovered by other methods than the SEREX technology like RDA (LAGE) or DNA cloning and expression in eukaryotes, using T lymphocyte clones as probes (CAMEL). The discovery of strong NY-ESO-1-specific immunity in individual cancer patients eventually led to the definition of HLA-class I restricted T-cell epitopes, opening new perspectives for the development of NY-ESO-1 directed cancer immunotherapy. The initial finding of strong humoral NY-ESO-1-specific immunity later was correlated with detectable NY-ESO-1-specific T-cell immunity in patients with tumors typing positive for NY-ESO-1. In NY-ESO-1 antibody negative patients, T-cell immunity may be induced by appropriate vaccination with secondary antibody induction in some patients. The conditions of induction of NY-ESO-1-specific immune responses, the biological impact of integrated immune responses with detectable antibody and T-cells and the consequences for the clinical outcome are central questions of a concerted effort, launched by the Cancer Research Institute and the Ludwig Institute for Cancer Research, through a worldwide cooperative network of cancer immunologists to exploit the potentials of NY-ESO-1-based cancer vaccination in a coordinated and supplementary way. Starting with MHC class I restricted peptide epitopes, a series of clinical cancer immunotherapy trials modified in a complementary fashion were initiated in patients with NY-ESO-1 positive cancers as determined by RT-PCR and immunohistochemistry. Later MHC class II restricted epitopes and variant epitopes with different MHC binding properties were also included to examine and exploit their potential in the induction and improvement of NY-ESO-1-specific immunity in cancer patients. Different adjuvants combined with peptide epitopes, whole NY-ESO-1 protein or recombinant viral NY-ESO-1 constructs have been launched. In parallel, advanced monitoring techniques have been established and refined to assess NY-ESO-1-specific immune responses in a standardized fashion, a crucial step, marking a new era in the development of antigen-specific cancer immunotherapy.

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