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Naturally occurring immunogenicity of NY-ESO-1 in cancer patients

Sacha Gnjatich

Ludwig Institute for Cancer Research, Memorial Sloan-Kettering Cancer Center, New York, NY

Abstract

There is ample evidence that the immune system recognizes and shapes the antigenic profile of tumor cells. However, as seen with AIDS, immune responses appear to fail to rid patients of disease. A comparison with successful antiviral or antibacterial vaccines emphasizes the requirement for defining immunogenic targets as the first step towards learning how to modulate immunity.

Germ cell antigen NY-ESO-1 was discovered as a consequence of its capacity to elicit spontaneous antibody responses in cancer patients (1). In a survey of sera from patients with various cancers, it was found that antibody responses to NY-ESO-1 were elicited only in patients with NY-ESO-1 tumor expression (2). Generally, NY-ESO-1 expression tends to be more frequent in advanced disease, and this is also seen with the humoral response to NY-ESO-1. NY-ESO-1 antibody titers drop following surgical resection of tumors, indicating that humoral responses are antigen driven (3).

NY-ESO-1 elicits CD8+ T-cell responses, as measured by mixed lymphocyte-tumor cultures (4), elispot (5) and tetramer (6) assays, or by a general method developed for assessing NY-ESO-1 responses in patients with any HLA haplotype (7). With only rare exceptions, CD8+ T-cell responses always occur in patients with NY-ESO-1 tumor expression and seropositive for NY-ESO-1 (5).

Defining the CD4+ T-cell responses to NY-ESO-1 is currently of much interest (8, 9, 10). Recently, a new technological development has allowed the analysis of CD4+ T-cell responses in single-cell based assays (11). As with CD8+ T-cell responses, CD4+ T-cell responses to NY-ESO-1 also correlate with antibody presence in the serum (12).

In conclusion, a subset of patients with NY-ESO-1 positive cancers develop strong spontaneous integrated multi-epitopic CD8+, CD4+, and antibody responses to NY-ESO-1. The challenges ahead involve correlating existing immunity to NY-ESO-1 with cancer progression and prognosis, and learning if patients with no NY-ESO-1 immune responses benefit from surrogate intervention by vaccination.

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