A MAGE-A4 peptide presented by HLA-A2 is recognized by cytolytic T lymphocytes

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The MAGE-encoded antigens that are recognized by cytolytic T lymphocytes (CTL) are shared by many tumors and are strictly tumor specific. Clinical trials involving therapeutic vaccination of cancer patients with MAGE antigenic peptides or proteins are in progress. To increase the range of patients eligible for therapy with peptides, it is important to identify additional MAGE epitopes. We have used a method to identify CTL epitopes, which selects naturally processed peptides. CD8(+) T cells, obtained from individuals without cancer, were stimulated with autologous dendritic cells infected with a recombinant adenovirus containing the MAGE-A4 coding sequence. Responder cell microcultures that specifically lysed autologous EBV-transformed B cells infected with vaccinia-MAGE-A4 were cloned using autologous stimulator cells infected with a Yersinia enterocolitica carrying the MAGE-A4 sequence. An anti-MAGE-A4 CTL clone was obtained and the epitope was found to be decapeptide GVYDGREHTV (amino acids 230-239) presented by HLA-A2 molecules. The CTL clone lysed HLA-A2 tumor cells expressing MAGE-A4. This is the first reported antigenic peptide encoded by MAGE-A4. It may be valuable for cancer immunotherapy because MAGE-A4 is expressed in 51% of lung carcinomas and 63% of esophageal carcinomas, whereas about 50% of Caucasians and Asians express HLA-A2.
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