Melanoma patients respond to a new HLA-A*01-presented antigenic ligand derived from a multi-epitope region of melanoma antigen TRP-2.

Abstract:

Tyrosinase-related protein-2 (TRP-2) is a known target antigen of spontaneous cytotoxic T cell responses in melanoma patients. Its frequent expression in metastatic tumors suggests that it might be an ideal candidate antigen for T cell-based immunotherapy. To provide knowledge about TRP-2-derived T cell epitopes useful for immunotherapy we applied a “reverse immunology strategy” based on repeated in vitro peptide stimulation of peripheral blood lymphocytes (PBL) from normal donors with predicted HLA-A*01 ligands. This led to the identification of TRP-2(181-190) as the first HLA-A*01-presented TRP-2-derived epitope. T-cell lines specific for peptide TRP-2(181-190) could be established from PBL of 50% of the normal HLA-A*01(+) donors tested. Such T cells responded specifically to autologous dendritic cells transduced virally with TRP-2, as well as to HLA-A*01(+) TRP-2(+) melanoma cells, although tumor cells had to be pretreated with IFN-gamma to become susceptible to T cell recognition. Interestingly, short-term in vitro peptide stimulation of PBL from HLA-A*01(+) melanoma patients showed the presence of TRP-2(181-190)-reactive CD8(+) T cells in some donors, suggesting their in vivo sensitization. Because TRP-2(181-190) overlaps with the known HLA-A*0201-presented epitope
TRP-2(180-188), an 11mer peptide encompassing both epitopes might be of specific value for vaccination of a broad population of melanoma patients.