Dendritic cells pulsed with RNA encoding allogeneic MHC and antigen induce T cells with superior antitumor activity and higher TCR functional avidity.

Abstract:
Adoptive transfer of T cells expressing transgenic T-cell receptors (TCRs) with antitumor function is a hopeful new therapy for patients with advanced tumors; however, there is a critical bottleneck in identifying high-affinity TCR specificities needed to treat different malignancies. We have developed a strategy using autologous dendritic cells cotransfected with RNA encoding an allogeneic major histocompatibility complex molecule and a tumor-associated antigen to obtain allo-restricted peptide-specific T cells having superior capacity to recognize tumor cells and higher functional avidity. This approach provides maximum flexibility because any major histocompatibility complex molecule and any tumor-associated antigen can be combined in the dendritic cells used for priming of autologous T cells. TCRs of allo-restricted T cells, when expressed as transgenes in activated peripheral blood lymphocytes, transferred superior function compared with self-restricted TCR. This approach allows high-avidity T cells and TCR specific for tumor-associated self-peptides to be easily obtained for direct adoptive T-cell therapy or for isolation of therapeutic transgenic TCR sequences.