



ORAL PRESENTATION

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Augmentation of donor-derived Tax-specific CTL responses by a novel Tax epitope-specific CD4⁺ helper T-cells in ATL patients after allogeneic hematopoietic stem cell transplantation

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Adult T-cell leukemia/ lymphoma (ATL) is an aggressive T-cell malignancy caused by human T-cell leukemia virus type 1 (HTLV-1) and characterized by extremely poor prognosis because of intrinsic drug resistance to cytotoxic agents. Recently, allogeneic hematopoietic stem cell transplantation (allo-HSCT) has been shown to be an effective treatment for ATL due to graft-versus-leukemia effects. However, donor-derived HTLV-1-specific T-cell responses in ATL patients after allo-HSCT are not well understood. In this study, blood samples from 15 ATL patients at 180 days following allo-HSCT from seronegative donors were screened for IFN- γ production of donor-derived T-cells against Tax protein. Among 15 patients, Tax-specific T-cell responses were observed in 11 patients. Direct detection with Tax/MHC class I tetramers revealed that donor-derived Tax-specific CD8⁺ cytotoxic T-lymphocytes (CTLs) were present in 12 of 15 patients. We then identified a novel Tax epitope (Tax155-167) presented by HLA-DR1 (HLA-DRB1*0101) and examined the presence of Tax-specific CD4⁺ T-cells in 3 HLA-DR1⁺ patients after allo-HSCT using a newly generated Tax155-167/HLA-DR1 tetramer. Tax155-167-specific CD4⁺ T-cells were found to be present in all HLA-DR1⁺ patients tested. Furthermore, in vitro stimulation of PBMCs from HLA-DR1⁺ HLA-A*2402⁺ patients with both Tax155-167 and HLA-A*2402-restricted CTL

epitope (Tax301-309) led to robust expansion of Tax301-309-specific CTLs. Our results suggest that donor-derived HTLV-1-specific both CD4⁺ and CD8⁺ T-cells could be induced in ATL patients after allo-HSCT from seronegative donors, probably due to exposure to HTLV-1 antigens from recipient-derived ATL cells, and the HTLV-1-specific CD4⁺ T-cells may contribute to efficient induction of donor-derived HTLV-1-specific CTL responses.

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