OA4-4

In Depth Investigation of Peripheral and Gut HIV-1 Reservoirs, HIV-Specific Cellular Immunity, and Host Microchimerism following Allogeneic Hematopoetic Stem Cell Transplantation

T. Henrich[1,2], E. Hanhauser[1], M. Sirignano[3], B. Davis[2,3], T.-H. Lee[4,5], S. Keating[4,5], M. Busch[4,5], F. Marty[1,2,6], A. LaCasce[2,6], P. Armand[2,6], R. Soiffer[2,6], M. Altfeld[2,3,7], D. Kuritzkes[1,2]
[1]Brigham and Women's Hospital, Boston, United States, [2]Harvard Medical School, Boston, United States, [3]Massachusetts General Hospital, Boston, United States, [4]Blood Systems Research Institute, San Francisco, United States, [5]University of California, San Francisco, San Francisco, United States, [6]Dana-Farber Cancer Institute, Boston, United States, [7]Ragon Institute of MGH, Harvard & MIT, Cambridge, United States

Background: We previously reported the loss of detectable peripheral blood HIV-1 reservoirs in 2 individuals following reduced-intensity conditioning allogeneic hematopoetic stem cell transplantation (RIC-alloHSCT) from wild-type CCR5 donors. To understand further the impact of alloHSCT on viral reservoirs, we studied the longitudinal effects of HSCT on host microchimerism and HIV-specific cellular immunity, and tested rectal tissue and peripheral blood mononuclear cells (PBMCs) obtained by leukapheresis for evidence of residual HIV-1 DNA or replication-competent proviruses up to 4.3 years post-transplantation.

Methods: The following experiments were performed: 1) collection of PBMCs by leukapheresis for large-scale HIV-1 quantification of genomic DNA and viral co-culture from purified CD4+ T lymphocytes (assays using 5 million PBMCs were repeated up to 30 times for each patient), 2) HIV-1 DNA PCR on rectal tissue (one patient), and 3) microchimerism studies of residual donor PBMCs. We also investigated HIV-specific cellular immune function by ELISpot IFN-gamma screenings of total PBMCs involving comprehensive HLA-specific peptide panels on the above patients in addition to a third RIC-alloHSCT patient that died 6 months post-transplantation from recurrent lymphoma; a fourth patient who received an autologous HSCT served as a control.

Results: No HIV-1 DNA was detected from PBMCs from both previously-reported RIC-alloHSCT patients indicating at least a 3 to 4 $\log_{10}$ decrease in peripheral viral reservoir size post-transplantation. No HIV-1 p24 antigen was detected by viral co-culture from purified CD4+ T cells, and no HIV-1 DNA was detected in rectal tissue. Residual host cells constituted less than 0.001% of PBMCs post-HSCT and may have represented circulating non-hematopoietic cells. No HLA-specific or pooled HIV-1 peptides elicited a strong HIV-specific immune response from all patients either before or after allogeneic or autologous HSCT.

Conclusion: HIV-1 remained undetectable from peripheral blood and rectal tissue after RIC-alloHSCT in patients on ART despite the testing of very large numbers of PBMCs or CD4+ T cells. The lack of detectable HIV-1 was in the setting of full donor chimerism and weak HIV-specific cellular immunity. Analytical treatment interruption remains the definitive experiment to test the full impact of RIC-alloHSCT on HIV-1 persistence.