Retrovirology

BioMed Central

Oral presentation

OA031-03. Increased regulatory T cell frequency and HIV-1 specific suppression after therapeutic vaccination of HIV-infected patients on antiretroviral therapy

BC Macatangay*[1], ME Szajnik[2], TL Whiteside[2], SA Riddler[1] and CR Rinaldo[3]

Address: [1]Division of Infectious Diseases, University of Pittsburgh, Pittsburgh, PA, USA, [2]University of Pittsburgh Hillman Cancer Center, Pittsburgh, PA, USA and [3]University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA, USA

* Corresponding author

from AIDS Vaccine 2009
Paris, France. 19–22 October 2009

Published: 22 October 2009

Retrovirology 2009, **6**(Suppl 3):O21 doi:10.1186/1742-4690-6-S3-O21

This abstract is available from: http://www.retrovirology.com/content/6/S3/O21

Background

We tested the hypothesis that therapeutic vaccination against HIV-1 can lead to an increase in the frequency and suppressive function of regulatory, CD4+ T cells (Treg).

Methods

HIV-1(+) subjects on ART (n = 17) were enrolled in a phase I therapeutic vaccine trial where they received 2 doses of autologous dendritic cells loaded with HIV-1 peptides. Peripheral blood mononuclear cells (PBMC) obtained from the subjects pre- and post-vaccine, and from normal controls (NC) were stained with antibodies specific for Treg (CD4+CD25hiFOXP3+), CD45RO, GITR, and CTLA4 and assayed by flow cytometry. PBMC pre and post-vaccine from 7 subjects were also evaluated for polyfunctionality using a flow cytometry-based, CD8+ T cell intracellular cytokine staining assay for 5 immune mediators after stimulation with Gag peptide, staphylococcal enterotoxin B (SEB) and medium alone. Treg were depleted in one set, and total vaccine response (post-vaccine - pre-vaccine) was compared in the Treg(+) and Treg-depleted (Treg-) sets.

Results

After vaccination, 12/17 subjects had increased Treg frequency from 0.74% to 1.2% (p = 0.06); the median increase was 30%. Of the 11 patients whose CD8+ T cells did not respond to the vaccine by an increase in production of interferon γ (ELISPOT assay), 7 (64%) had increased frequencies of Treg. Although there was no significant change in CD8+ T cell polyfunctionality after vaccination, depletion of Treg resulted in increased polyfunctionality post-vaccine (p = 0.029), with the percentage of CD8+ T cells producing more than 1 immune mediator increasing to more than twice the pre-vaccine levels. There was no difference in polyfunctionality in the Treg(+) and Treg(-) sets when stimulated with SEB, implying specificity of suppression to HIV-1 antigens.

Conclusion

Therapeutic immunization against HIV-1 causes a modest increase in Treg frequency and a significant increase in HIV-1-specific, Treg suppressive function. The role of Treg should be considered in immunotherapeutic trials of HIV-1 infection.