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Polyvalent immune responses correlate with lower number of HIV infected CD4 T-cells in chronically infected subjects treated with autologous RNA pulsed DC therapy

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Background: AGS-004 immunotherapy consists of autologous DCs electroporated with autologous amplified HIV RNAs (Gag, Vpr, Rev and Nef). AGS-004 was administered every four weeks to chronic HIV patients while on standard antiretroviral therapy (ART). At week 14, after 4 administrations a 12-week analytical treatment interruption (ATI) began, during which AGS-004 dosing continued every four weeks. Thirty six participants completed ATI, 23 of whom received AGS-004. This study evaluated the impact of AGS-004 on the level of integrated HIV DNA (pDNA) in CD4 T cells and its correlation with the immune response.

Methods: Peripheral blood samples were collected during a clinical study at baseline, week 8 during ART treatment and week 18 and week 26 during ATI. PBMCs were isolated using Ficoll separation and CD4 T cells were isolated using negative selection with a human CD4+ T Cell Isolation kit (Miltenyi). Genomic DNA was isolated using the Gentra Puregene kit (Qiagen). 15,000 genomes were used in a repetitive Alu-Gag based PCR. pDNA analysis was conducted on 35 subjects. Immunomonitoring data was available on 32 subjects. Levels of pDNA were correlated with the magnitude and quality of immune responses for 31 subjects. Immunomonitoring was conducted to determine if HIV-specific immune responses were generated. The analysis was conducted against all four or individual antigens used in AGS-004.

Results: There were no differences in pDNA levels in immunized versus placebo subjects (N=35). However, in an analysis of AGS-004-treated subjects (N=21), HIV pDNA levels were significantly lower in those subjects who developed multifunctional memory T cell responses (N=14) after two, five or seven doses of AGS-004 (weeks 8, 18 and 26) but not at baseline. The attenuation of pDNA levels were not associated with immune response to any individual antigen. These data taken together indicate that a polyvalent immune response directed against multiple antigens is important for the control of pDNA levels in CD4 T cells.

Conclusions: The results of this study provide a rationale to combine AGS-004 with ART and a latency reversing agent for the purpose of boosting the immune response to eliminate HIV reservoirs in infected individuals.

HIV-speciî€Ÿc CD4 responses contribute to the high immune activation observed in PHI. Twenty-seven patients with early PHI were included in a prospective longitudinal study. and 12 of them received ART after enrollment. Fresh peripheral blood mononuclear. cells were used for measurement of ex vivo T-cell activation and of cytokine-producÂ Patients with lower immune activation exhibited higher. frequency of bulk CD4 T-cells producing IFN-Î³ or IL-17 and higher effector-to-regulatory. cell ratios. No differences were found in HIV-speciî€Ÿc CD4 T-cell frequencies. In contrast, segregation of patients based on plasma viral load (pVL) revealed that patients with.Â of CD8 T cells to control HIV viral replication, CD4 T cells have long been neglected as eî€žectors in. 2. Chevalier et al. CD4 T-cells are considered "helper" cells because they do not neutralize infections but rather triggers the body's response to infections.Â In doing so, the host CD4 cell is killed. The infected person's ability to trigger an immune defense is gradually depleted to such a point as to leave their body open to opportunistic infections. The dynamics of HIV are such that "killer" CD8 T-cells are increasingly left blind in an advancing infection and eventually become unable to cope with the growing population of HIV (as measured by the viral load). If an HIV infection is left untreated, the immune system will, in all but rare cases, completely collapse (or become compromised). Types of CD4 T-Cells. More often than not we HIV-1 virus-like particles (VLPs) are promising vaccine candidates against HIV-1 infection. They are capable of preserving the native conformation of HIV-1 antigens and priming CD4+ and CD8+ T cell responses efficiently via cross presentation by both major histocompatibility complex (MHC) class I and II molecules. Progress has been achieved in the preclinical research of HIV-1 VLPs as prophylactic vaccines that induce broadly neutralizing antibodies and potent T cell responses. Moreover, theâ€¦ CONTINUE READING. CD8+ T-Cells as Correlates of Immune Reconstitution During Antiretroviral Therapy. CXCR5+ CD8+ T-Cells and Their Role During HIV Infection. CD8+ T-Cell-Based Strategies To Treat Or Cure HIV Infection.Â Importantly, the success of cART in reducing AIDS-related deaths and increasing the life expectancy of HIV-infected patients, has resulted in a high number of patients over 50 years living with HIV (available at https://www.cdc.gov/hiv/group/age/olderamericans/index.html). Thus, the presence of concomitant diseases, such as metabolic or cardiovascular pathologies, and their respective medications, influence the choice of antiretroviral drugs for cART regimens, and increase the risk of side effects due to drug interactions (12).