Therapeutic vaccine trials

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HIV-1 reservoir dynamics after vaccination and antiretroviral therapy interruption are driven by dendritic cell-vaccine induced T-cell responses

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Background: We recently reported a peak decrease of viral set-point of 1.2 log10 associated with an increase in HIV-1-specific T cell responses in HIV infected individuals receiving autologous myeloid derived dendritic cells (MDDC) pulsed with autologous heat-inactivated whole HIV. Here we assessed if the HIV specific immune responses induced by the vaccine might have cleared some of the reservoir and drove the dynamics of replenisment of viral reservoir during the antiretroviral therapy (cART) interruption.

Methods: We measured total and integrated HIV-1 DNA in isolated CD4 T cells in 36 patients on cART randomized to receive 3 immunizations with MDDC pulsed with autologous HIV-1 (n=24) (DC-HIV-1) or with non-pulsed MDDCs (n=12) (DC-control) at 6 time-points: before any cART, before STOP1 (a first cART interruption 56 weeks before the first immunization to isolate virus for pulsing MDDCs), before and after vaccinations (VAC1 and VAC2) and at weeks 12 and 48 after second interruption of cART.

Results: Vaccinations did not influence HIV-1 DNA levels in vaccinated subjects. After cART interruption post-vaccination (week 12), while total HIV-1 DNA significantly increased in both vaccinees (n=24) and controls (n=12), integrated HIV-1 DNA did not change in vaccinees (1.8 to 1.9, p=0.22) and increased in controls (1.8 to 2.1, p=0.05) (p=0.03 for the difference between groups). HIV-1 specific T cells responses at VAC2 time-point were strongly and inversely correlated with total and integrated HIV-1 DNA after vaccination (r= -0.46, p=0.04 and r= -0.79, p< 0.0001, respectively) and after cART interruption in vaccinees (r= -0.69, p=0.002 and r= -0.82, p< 0.0001, respectively), while a direct correlation was observed in DC-controls (r= 0.72, p=0.03 and r= 0.67, p=0.05 total and integrated HIV-1 DNA after vaccination, respectively) and no correlations were found after cART interruption). These associations were mainly observed with HIV-1 specific T cell responses targeting gag p24 and p17 and nef antigens.

Conclusions: HIV-1 specific T cell immune responses elicited by therapeutic DC vaccines could drive changes in viral reservoir after vaccination and the replenishment of reservoir after cART interruption in chronic HIV-1 infected patients treated at early stages.