Immune activation and defective pTfh are associated with impaired immunity in aging HIV+ persons

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ABSTRACT

Background: With improved antiretroviral treatment (ART) and increasing life expectancy, the aging HIV+ population is rising. HIV+ vaccine design and aging are independently associated with worse immune responses to 

Methods: The study represents initial observations from a larger ongoing study in young (Y) and old (O) 50 years or more (n=48) in Miami, FL. Four groups n=12 each (Y+, Y-, O+, O-) were HIV- and showed viral load >200 copies/mL in the previous 12 months. Asymptomatic HIV+ persons were identified by enrollment into a 2013 influenza vaccination trial and had CD4+ T cell counts >350 cells/µL. Groups were stratified according to presence of ART and known ART exposure. Exogenous IG (50 µg) and non-IG (see Table 1) vaccines were administered as 2 doses at 21 days (T0, T2) and 4 weeks post-vaccination (T2). Blood was obtained at T0 and T2 for baseline PBMC isolation for IFN-γ Release Assays and flow cytometry. Lymphocytes were characterized for CD4+ and CD8+ T cell activation and further analyzed for HIV-specific antibody responses at T2.

RESULTS

- Response to vaccination was measured as percentage of memory B cell responses at T2 compared to T0.

- T2 responses were compared to T0 responses using the Wilcoxon signed-rank test.

- Differences were considered significant if p<0.05.

- Summary: 48 participants T2 each of Y+, Y-, O+, O- showed significant increase compared to T0. Y+ showed increased HIV-specific humoral responses compared to Y- and O-, primarily due to enhanced HIV-specific antibody responses at T2.

- O- showed highest baseline CD4 T cell activation immune response (similar to Y+); both groups showed enhanced immune responses to NK cell activation and influenza vaccination.

- At 4 wk post vaccination, Y+ showed enhanced IFN-γ, IL-12 and IL-10 production compared to Y- and O-, and O- showed highest baseline CD4 T cell activation compared to Y-. Baseline CD4 T cell responses at T2 were significantly correlated with HIV-specific antibody responses.

- Exogenous IL-21 enhanced total IgG responses in all Y+ and O- vaccine groups compared to baseline. HIV-specific memory B cell responses were enhanced in all Y+ vaccine except O- when compared to baseline.

CONCLUSIONS

- Antibody responses to seasonal influenza vaccination are independently associated with aging and immune response. These responses are correlated with HIV- old people despite ART with stringent vaccination and CD24 reconstitution implying that both HIV and aging contribute to immune deficiency in HIV+ aging population.

- Impaired vaccine responses are associated with underlying immune activation coupled with deficient pTfh and HIV specific antibody responses at T2 to decrease immune activation and to augment Th1 responses, which may be helpful in improving immune responses in the HIV+ and aging population.

REFERENCES


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STUDY POPULATIONS

- Study population: 48 participants, all women, age (O) 57±21 (premenopausal) and young (Y) 15±45 (HIV+ and HIV negative). All were on ART except those with baseline CD4 T cell counts >350 cells/µL. All were HIV- and had viral load >200 copies/mL in the previous 12 months. Exogenous IG (50 µg) and non-IG (see Table 1) vaccines were administered as 2 doses at 21 days (T0, T2) and 4 weeks post-vaccination (T2).

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