Retrovirology

Poster presentation

P04-48. HIV-1 envelope induces memory B cell responses that correlate with plasma antibody levels after gp120 protein vaccination or chronic HIV-1 infection

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Background

Successful vaccines (e.g. tetanus) can induce long-lived antibody levels that are maintained by long-lived plasma cells and do not correlate with numbers of blood memory B-cells. Early events during HIV-1 acute infection may impair the timely onset of neutralizing antibody responses. Thus, an effective HIV-1 vaccine should elicit high levels of durable antibodies by long-lived plasma cells. We asked if HIV-1 envelope-specific memory responses are sustained by memory B-cells in the settings of HIV-1 gp120 envelope vaccination and chronic HIV-1 infection (CHI).

Methods

Total, gp140 envelope and V3-specific IgG memory B-cells from PBMCs of 26 CHI patients and 25 vaccinated volunteers from the VaxGen clinical trial VAX004 were enumerated with ELISpot assays after *in vitro* stimulation. Respective plasma antibody levels were tested with ELISA. An additional 8 CHI subjects, treated with ART for between 125 and 387 weeks and with viremia suppression, were studied for levels of anti-gp120, -gp41, -p55, -tetanus toxoid and -influenza IgG plasma antibodies (Luminex assay and ELISA) over time of ART to determine the relative antibody level half-lives.

Results

Levels of anti-HIV-1 envelope plasma antibodies and memory B-cells correlated both in CHI and vaccinated individuals. Moreover, whereas the reported expected half-life of plasma antibody levels to protein vaccines is >10 years when maintained by long-lived plasma cells (we observed ~11 years for tetanus), plasma anti-envelope antibody level half-lives were ~33–81 weeks in ART-induced aviremic CHI subjects. In contrast, anti-p55 Gag antibody level half-life was 648 weeks and antibody titers against influenza did not decay in-between yearly or biennial influenza vaccine boosts.

Conclusion

These data demonstrated that HIV-1 envelope induces predominantly short-lived memory B-cell-dependent plasma antibodies in the settings of envelope vaccination and chronic HIV-1 infection. The inability to generate high titers of long-lived anti-envelope antibodies is a major hurdle to overcome for the development of a successful HIV-1 vaccine.