Retrovirology

Poster presentation

P17-22. Impact of rare adenovirus seroprevalence on HIV-1 acquisition in the Step study

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Background

In the phase IIb Step study, vaccinees with baseline Ad5-specific neutralizing antibodies (NAbs) exhibited a potential increased rate of HIV-1 acquisition as compared with placebo controls. We sought to evaluate whether baseline Ad5 NAbs correlated with NAbs to non-type C rare Ad serotypes and whether baseline NAbs to rare Ad serotypes correlated with enhancement of HIV-1 acquisition after rAd5-gag/pol/nef vaccination.

Methods

In a case-controlled study, baseline sera from 81 cases who acquired HIV-1 infection during the Step study (52 vaccinees and 29 placebo recipients) and 324 non-cases who did not acquire HIV-1 infection (208 vaccinees and 29 placebo recipients) were evaluated for Ad5, Ad26, Ad35, and Ad48 NAb titers. Non-cases were randomly selected and matched for treatment arm, Ad5 serostatus, circumcision status, and geographic region.

Results

Baseline Ad5 seroprevalence was 58% in these samples with a median titer of 702. In contrast, baseline Ad26, Ad35, and Ad48 seroprevalence was 14%, 6%, and 17%, respectively, with median titers of 49, 47, and 46. There were no correlations between baseline Ad5 NAbs and Ad26/35/48 NAbs (P = 0.44–0.77, Spearman rank correlation tests). Moreover, there were no differences observed in baseline Ad26/35/48 NAbs between cases and non-cases (P = 0.46–0.97, Wilcoxon rank sum tests).

Conclusion

Ad5 NAbs and Ad26/35/48 NAbs were independent variables that did not co-segregate, indicating that Ad5 NAbs were not a surrogate marker for and did not predict NAbs to these rare Ad serotypes. In addition, no increased HIV-1 acquisition was observed in subjects with baseline Ad26/35/48 NAbs following rAd5 vaccination. These data suggest that cross-reactive immunity against heterologous Ad serotypes did not contribute to increased HIV-1 susceptibility in this study. These findings have important implications for the development of rare serotype Ad vector-based vaccines for HIV-1.

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