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Poster presentation

P16-09. Adenovirus 5 vector HIV vaccination does not affect mucosal homing markers on Ad5-specific CD4+ T-cells in humans

N Hutnick*[1], D Carnathan[1], S Dubey[2], K Cox[2], S Ratcliffe[1], MN Robertson[2], DR Casimiro[2], HC Ertl[3] and MR Betts[1]

Address: [1]Microbiology, University of Pennsylvania, Philadelphia, PA, USA, [2]Merck Research Laboratories, West Point, PA, USA and [3]Wistar Institute, Philadelphia, PA, USA

* Corresponding author

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Background

The reasons for the recent failure of the Merck STEP trial, wherein Ad5-seropositive subjects demonstrated increased susceptibility to HIV infection, remain unclear. One potential hypothesis is that expansion and mucosal trafficking of Ad5-specific CD4+ T cells following Ad-vector immunization possibly rendered vaccinees more susceptible to HIV infection.

Methods

Ad-specific T cell responses were characterized in five seropositive and seronegative subjects from the Merck phase I 016 trial, the immediate STEP trial predecessor. Subjects received 3 × 1011 vector particles Merck Ad5 gag/pol/nef at weeks 0, 4 and 30. PBMC samples were obtained at weeks 0, 4, 8,18, 26, 30, 42, 52 and 78 relative to vaccination. T-cell responses to Ad were measured by stimulating PBMCs overnight with whole Ad vector before measuring functionality (IFN-γ, TNF-α, IL-2) memory phenotype (CD45RO, CCR7) and mucosal homing markers (α4, β7, CCR10, αE) by multicolor flow cytometry.

Results

There was no difference in the % of total or Ad-specific α4+β7+ CD4+ T-cells between seronpositive and seronegative subjects. There was also no increase in total or Ad-specific α4+β7+ CD4+ T-cells following vaccination. Ad-specific CD4+ T-cells comprised only 1–2% of total α4+β7+ cells in the blood. The memory phenotype of α4+β7+ was mixed between central memory, effector memory and effector CD4+ T-cells in both serogroups with no change in memory phenotype observed upon vaccination. CCR10 and CD103 were expressed at marginal levels on Ad-specific CD4+ T cells.

Conclusion

This data suggests that vaccination does not induce a differential measurable effect on mucosal trafficking in circulating Ad-specific CD4+ T cells between the serogroups and therefore contradicts a role for Ad-specific T-cells in the possible increased risk of HIV infection observed during the STEP trial.