Retrovirology

Poster presentation

P11-09. Mucosal vaccination with a transferrin-gp140 conjugate via the nasal but not vaginal route elicits robust systemic and vaginal IgG and IgA responses

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Background

Mucosal anti-HIV immunity at the virus portal of entry is likely essential to protect against sexual transmission of HIV. While the female genital tract has some immune-inductive potential, responses elicited to vaccine antigens applied to the vaginal mucosae have been modest at best. Immunological linkage between nasal and vaginal MALT has been demonstrated in both mouse and man, suggesting that nasal vaccination may promote vaginal mucosal immunity. We used a novel transferrin receptor targeted vaccine conjugate to enhance delivery of a vaccinating antigen across the mucosal epithelial barrier and compared nasal with vaginal vaccination.

Methods

We conjugated trimeric Clade C HIV-gp140 to human transferrin (Tf) using a streptavidin-biotin linkage. Conjugate formation was characterized by SDS-PAGE and size analysis then topically administered nasally or vaginally to medroxyprogesterone-treated mice with or without previous unadjuvanted gp140 systemic priming. Serum and vaginal lavage samples were collected and tested by ELISA for anti-HIV-gp140 specific IgG and IgA.

Results

Unconjugated HIV-gp140 administered to either the vaginal or nasal mucosa was insufficient to generate antigen-specific responses. However, the Tf-gp140 conjugate elicited antigen-specific IgG responses in serum after nasal administration. A systemic prime followed by either a vaginal or nasal mucosal boost vaccination significantly enhanced antigen-specific serum IgG, with the Tf-gp140 conjugate being more effective than antigen alone. Importantly, a systemic gp140 priming vaccination followed by nasal Tf-gp140 conjugate boosts generated robust gp140-specific vaginal mucosal IgG and IgA antibody responses.

Conclusion

The comparison of the utility of nasal or vaginal mucosae as immune-inductive sites demonstrated that vaccination via the nasal but not the vaginal route elicited strong vaginal IgG and IgA responses. Our novel conjugate, that delivers vaccine antigens by transcytosis to sub-mucosal compartments where immune cells reside, highlighted the difference between the immune-inductive potential of these two mucosal sites.