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Poster presentation

P19-02. High protection of female macaques from repeated intravaginal challenges with SHIV-162P3 upon mucosal vaccination with Gp41 subunits-virosomes

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Background

IDS is mainly a sexually transmitted infection. Blocking sexual transmission of HIV requires developing a prophylactic vaccine that promotes a protective mucosal response in genital and intestinal compartments for preventing initial HIV transmission events. Induction of such long lasting mucosal response requires developing a mucosal vaccine strategy.

Methods

We have developed a mucosal vaccine candidate based on two complementary conserved gp41 subunit antigens- a trimeric recombinant gp41 deleted in known immunodominant regions (rGp41) and the 35 amino acid peptide P1, this later adopting the 3D conformation of the gp41 MPER and target of HIV-neutralizing IgA in highly exposed but persistently seronegative individuals- for focusing the immune response on relevant neutralizing epitopes. Gp41 subunit antigens are grafted on virosomes, a market-approved vaccine carrier with intrinsic adjuvant properties. Female Macaca mulata were immunized 4 times with both rGp41- and P1 peptide-virosomes, using either the sole intra-muscular or the combined intra-muscular/intra nasal routes. Five weeks post-vaccination, animals were challenged 13 times intra-vaginally with low dose of SHIV162p3 at a biweekly frequency.

Results

Up to 13 weeks post-challenge, 5/5 animals vaccinated by the combined intra muscular/intra nasal routes were fully protected against SHIV162p3 (undetectable viremia, anti-HIV IgG seronegativity), as compared to the 6/6 infected control group, or the 5/6 infected animals vaccinated by only the intra muscular route. Protection was correlated to gp41-specific IgA in vaginal secretions with *in vitro* neutralizing activities against transcytosis and CD4+ cell infection.

Conclusion

Mucosal IgA specific for gp41 could block the initial steps of HIV transmission at the female genital tract, by blocking either HIV entry by transcytosis in the epithelium or infection of immune cells in the submucosa. Virosome-gp41 subunit vaccines raising a mucosal antibody response against key epitopes of gp41 that control HIV infection and transcytosis could provides a mucosal protection against sexual HIV transmission.