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Improved systemic and mucosal antibody responses with a CCR10 ligand adjuvant

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Background

The induction of potent mucosal immune responses will be critical for an effective HIV vaccine, However, a major limitation of current vaccine development is the ability to induce mucosal antibodies by a systemic, non-replicating vector. To address this inadequacy, we have hypothesized that encoding instructions for immune cell targeting to the mucosa in the form of MEC, a mucosal chemokine adjuvant delivered as a plasmid can redirect immune responses in vivo. MEC (CCL28) is normally expressed by epithelium in the skin, lungs, and intestines and it functions to attract CCR10 expressing plasmablasts locally.

Methods

IIndian rhesus macaques were vaccinated using EP delivery with either a pcon SIVmac239 gag, pol, SIVsm unmatched E660 env vaccine delivered IM alone (n=5), with CCL28 (MEC, n=5) or a plasmid expressed H1 HA Influenza vaccine alone (n=4) or with MEC (n=4). SIV Vaccinated animals and 6 naïve controls were challenged vaginally twice weekly for four weeks with 500TCID50 SIVsmE660.

Results

The inclusion of a CCR10 ligand adjuvant enhanced vaginal and serum IgG and IgA titers compared with DNA alone. In Flu vaccinated animals functional HAI antibody titers were significantly elevated and above the 1:40 titer required for protection in humans with just a single dose of H1HA delivered with the MEC adjuvant. Following SIV challenge monkeys vaccinated with a CCR10 adjuvant showed 89% protection from the establishment of infection compared 40% with DNA alone with only 16% of the naïve animals.

Conclusion

Mucosal and systemic antibody responses were enhanced with the inclusion of a CCR10 ligand adjuvant. Dose sparing was also observed. DNA vaccination alone improved challenge outcome, and this was further enhanced by the inclusion of a CCR10 ligand adjuvant. The inclusion of mucosal homing chemokines represents a novel approach to induce improved mucosal immune responses by non-live systemic immunization of relevance to HIV infection.

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