Retrovirology

Poster presentation

P13-07 LB. A human blocking antibody to CCR5 partially protects against lentiviral infection in non-human primates

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Background

Transmission of HIV-1 is highly dependent on its co-receptor, CCR5, and humans with homozygous mutations in this gene product are protected relative to heterozygotes or wild type genotypes. Therefore antibodies to CCR5 might prevent establishment of HIV infection and help to define a potential cellular vaccine target. Here, we evaluate the ability of HGSmAb004 and HGSmAb101, two blocking human monoclonal antibodies to CCR5, to prevent SHIV 162P3 infection and stimulate HIV-1 immune responses in non-human primates.

Methods

The antibodies (10-40 mg/kg) were passively administered to rhesus macaques one day before mucosal challenge with SHIV SF162P3. Plasma viral loads, CCR5 mAb serum levels, and receptor occupancy were monitored regularly in these monkeys. The presence of SHIV-specific cellular immune responses was assessed in these monkeys by intracellular cytokine staining, and anti-SHIV antibodies were also detected by ELISA.

Results

Administration of HGSmAb004 reduced availability of CCR5 receptors by 90 to 100% in recipient animals. Passive transfer of this antibody blocked SHIV infection in two out of four monkeys and led to lower levels of viremia in the other monkeys, whereas HGSmAb101 led to lower viremia but not complete protection in monkeys from SHIV162P3 infection. Infected monkeys generated anti-SHIV specific cellular and humoral responses while uninfected monkeys developed little systemic long term memory T cell responses. One of the uninfected monkeys was protected from infection when it was rechallenged with the same virus in the absence of CCR5 mAbs and had low levels of systemic SHIV-specific T cell responses. In contrast, anti-viral cellular immunity was detected at a mucosal site by bronchoalveolar lavage.

Conclusion

Passive transfer of CCR5 antibodies can confer partial protection against a mucosal challenge with a CCR5-tropic SHIV virus in non-human primates and may allow the generation of anti-viral mucosal T cell immunity in protected animals.