Retrovirology

Poster presentation

P19-38. Safety and protective immunity in Rhesus monkeys immunized with replication-defective HIV/SIV vaccine

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Background

Live attenuated simian immunodeficiency virus (SIV) elicited the best protective immunity in rhesus monkeys. However, this vaccine approach was hindered by safety concerns that the live attenuated HIV-1 may cause harms in humans. To overcome this problem, we have developed a replication defective HIV/SIV pseudotyped with Vesicular Stomatitis Virus G protein (VSV-G) as an AIDS vaccine model.

Methods

In the vaccine construct, the polymerase, *vif*, *nef* and *env* genes of HIV/SIV were truncated. Replication defective viruses were produced by co-transfecting vaccine constructs with constructs encoding functional *pol* and *VSV-G* genes. Rhesus monkeys were immunized with replication-defective HIV/SIV through subcutaneous and intramuscular routes and monitored for replication competent virus (RCV) at weekly intervals in the first month and monthly in the following year. Sixty-seven weeks after immunization, three SIV vaccine immunized animals and two naïve controls were challenged with SIVmac via IV route. Two persistent infected monkeys also received therapeutic vaccines. Immunological responses were monitored during vaccination and challenge phases.

Results

No RCV was detected at any time-points during 67 weeks. Furthermore, no side effect was occurred in all vaccinated monkeys. After challenging, all immunized animals and naive controls have positive transient viremia. However, virus load becomes undetectable in the vaccinated animals two months after challenge by sensitive co-culture and PCR as compared to high viral loads in control animals for over one year. The level of CD4 cells also maintains at normal level in all vaccinated animals as compared to 60% drop in control animal. Viral load was significant reduced (>100-fold) in two monkeys received therapeutic vaccines.

Conclusion

The studies indicate that replication-defective HIV/SIV is safe and elicits long lasting protective immunity in rhesus monkeys. The protection is correlated to cell-mediated immune responses. Therefore, replication defective HIV-1 may provide a safe vaccine candidate for human clinical trials.