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Optimizing delivery of HIV-1 conserved region-derived immunogen for induction of T and B cell responses in rhesus macaques

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Background

The complexity of candidate HIV-1 vaccine formulations is increasing due to extreme challenges faced when trying to prevent or control HIV-1 infection.

Methods

Immunogen HIVconsv based on the most conserved regions of the HIV-1 proteome was used to explore combinations of seven distinct vaccines modalities in heterologous prime-boost regimens delivered to rhesus macaques to optimize induction of T cell and antibody responses. These include plasmid DNA (P), Semliky Forest virus replicons delivered as DNA (DREP; D) or virus particles (VREP; V), modified vaccinia virus Ankara (MVA; M), adenoviruses of human (HAdV-5; A) and chimpanzee origin (ChAdV-63; C) and adjuvanted synthetic long peptides (SLP; S).

Results

A number of observations were made. Thus, a very potent combination for induction of HIV-1-specific T cells was an adenovirus vector (A or C) followed by poxvirus M. S boost broadened T cell responses, but did not prime T cells efficiently. D was a stronger prime than P. PPP was the best prime for T cells, while PSS was best for induction of antibodies. Even very complex regimen PPPAMSSCMV continued to recruit new T cell clones into the response to a single epitope, although a ceiling for immunodominant responses was reached; subdominant responses could be boosted up to the last V delivery. Finally, PPSS, but not SSSS could protect 2/6 animals from SIVmac251 acquisition.

Conclusion

These results will guide initial design of human trials. So far, human studies in Oxford testing CM, PPPCM and PPPMC regimen concur with observations made in rhesus macaques.

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