

Oral presentation

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VSV/MVA vaccine rapidly elicits SIV antibodies and local and systemic SIV T cell responses in macaque neonates but does not prevent SIV dissemination after oral challenge

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Background

Despite availability of antiretroviral therapies, a neonatal vaccine is needed to prevent HIV-1 breast milk transmission in resource-poor settings. Given the relative immaturity of the infant immune system and the frequent, long-term exposure to HIV in breast milk, a neonatal HIV vaccine must induce quick, strong, and long-lasting anti-HIV immunity. Our prior studies demonstrated that intramuscular immunization with attenuated poxvirus-based SIV vaccines gave infant macaques partial protection against oral SIV challenge. We hypothesized that a vaccine vector that can replicate after oral administration may induce better mucosal immunity and be more effective.

Objectives

To test the safety, immunogenicity and efficacy of a recombinant vesicular stomatitis virus (VSV)-SIV gag, pol env (SIVgpe) prime/modified vaccinia Ankara (MVA)-SIVgpe boost vaccine regimen in infant rhesus macaques.

Materials and methods

VSV-SIVgpe was orally administered at birth, followed by intramuscular injection with MVA-SIVgpe at 2 weeks of

age to eight rhesus macaques. All vaccinated and eight unvaccinated infant macaques were challenged at 4 weeks of age by a repeated oral low-dose SIVmac251 inoculation regimen to mimic breast milk exposure. Lymphocyte subsets and SIV-specific T cell responses were assessed by multiparameter flow cytometry. Antibody levels were measured by whole SIV-lysate and SIV gp130 env ELISAs. SIV RNA levels were measured by SIV branched chain DNA assay.

Results

The VSV/MVA-SIVgpe vaccine elicited SIV-specific plasma antibodies (IgG and IgA) as well as CD4+ and CD8+ T cell responses in several oral and systemic lymphoid tissues. Despite the persistence of SIV-specific antibodies and T cell responses after SIV challenge, these responses were insufficient to prevent rapid virus dissemination. Plasma viral RNA levels in most vaccinates were indistinguishable from controls. Vaccinates with highest SIV gp130 antibody levels at the time of oral SIV infection had lowest viremia. Although few SIV-specific CD8+ T cells were observed, these cells were activated and had cytotoxic activity (CD107 expression after in-vitro SIV antigen stim-

ulation). T cell activation in tonsils was associated with lower numbers of regulatory T cells in this tissue.

Conclusions

Although this oral + injected SIV vaccine regimen succeeded in rapidly eliciting virus-specific antibodies and T cell responses in neonatal macaques, these immune responses did not limit virus dissemination after oral SIV inoculation. These data underline some of the challenges a vaccine must overcome to protect against HIV breast milk transmission

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