Early treatment with neutralizing antibodies is critical for preventing persistent infection in a macaque model of pediatric HIV-1

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Mother-to-child HIV transmission is a global health challenge

HIV-1, the virus that causes AIDS, is passed from mothers to their babies mainly during childbirth and breastfeeding. In industrialized countries, transmission has been nearly eliminated through the use of effective interventions, including antiretroviral drug therapy, Cesarean section delivery, and formula feeding. However, in many parts of the developing world, mothers and their infants have inadequate access to these resources. Thus, mother-to-child HIV-1 transmission is still prevalent; each year 150,000 infants are newly infected. In particular, there is an unmet need for a short-term treatment that would enable safer breastfeeding in the absence of a daily drug regimen.

A promising approach: neutralizing antibodies

Neutralizing anti-HIV antibodies bind to HIV-1 Env and block the virus from infecting cells. They can also recognize HIV-1-infected cells, and tell the immune system to destroy them.

- In animal models, treating with neutralizing antibodies before viral exposure can prevent infection.
- Efficacy is poor during chronic infection because HIV-1 establishes a persistent reservoir of long-lived, latently-infected cells, which are “invisible” to the antibodies.

The efficacy of antibodies during early infection (soon after exposure) has not been studied.

- If early treatment effectively blocks the establishment of latent reservoirs in infants, it could be a promising strategy for preventing mother-to-child HIV-1 transmission.
- Antibodies have a long half-life, so they could also protect the baby from infection during breastfeeding.

We used a macaque model of pediatric HIV-1 infection to ask:

Can post-exposure neutralizing antibody therapy prevent the establishment of persistent infection in infants?

Study Designs and Results

Treatment 24h after exposure prevents establishment of SHIV infection

Neutralizing antibodies: PGT121 and VRC07-523

Viral spread is rapid in early infection; Virus in tissues is cleared with antibodies within 2 weeks

Conclusions and Future Directions

- Prompt antibody treatment is essential for optimal efficacy in infants.
  - When given within 24 hours of exposure, neutralizing antibody therapy is effective in preventing the establishment of SHIV infection.
  - When antibody therapy was delayed an additional 24 hours, 5/6 animals had attenuated viremia, but reservoir establishment was not reliably prevented.
- Antibody therapy cleared the virus from tissues within 2 weeks.
  - What is the mechanism of clearance? Do antibodies directly kill infected cells? Or do they only halt viral dissemination, preventing re-seeding of the reservoir?
- Would a short course of antiretroviral therapy lengthen the effective treatment window for antibody therapy?
- Future work will examine the dynamics of SHIV reservoir establishment and antiviral defense in newborn macaques, with and without treatment.