

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 viral spike Virus: SHIV_{SF162P3} ELIMINATION OF MOTHER TO CHILD TRANSMISSION (weeks) Neutralizing antibodies: Oral SHIV_{SE1} **PGT121** and **VRC07-523** Treatment 24h after exposure prevents establishment of SHIV infection Source: UNICEF Cell-associated (PBMC) virus Plasma virus HIV-1, the virus that causes AIDS, is passed from mothers to their 10 mg/kg 10 mg/kg babies mainly during childbirth and breastfeeding. In industrialized of pl countries, transmission has been nearly eliminated through the use CD8 of effective interventions, including antiretroviral drug therapy, Cesarean section delivery, and formula feeding. However, in many parts of the developing world, mothers and their 40 mg/kg 40 mg/kg(copi infants have inadequate access to these resources. Thus, mother-toido . child HIV-1 transmission is still prevalent; each year 150,000 infants Ü RN are newly infected. In particular, there is an unmet need for a → 33309
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↔ 33308 SIV short-term treatment that would enable safer breastfeeding in the . **.** . . absence of a daily drug regimen. Time (weeks) A promising approach: neutralizing antibodies Viral spread is rapid in early infection; Neutralizing anti-HIV antibodies bind to HIV-1 Env and block the Virus in tissues is cleared with antibodies within 2 weeks virus from infecting cells. They can also recognize HIV-1-infected cells, and tell the immune system to destroy them. Day 1-2 Day 7 **Day 14** No treatment Buccal mucosa In animal models, treating with neutralizing antibodies before viral exposure can prevent infection. Efficacy is poor during chronic infection because HIV-1 Neutralizing establishes a persistent reservoir of long-lived, latently-infected antibody cells, which are "invisible" to the antibodies. therapy The efficacy of antibodies during *early* infection (soon after exposure) has not been studied. • If early treatment effectively blocks the establishment of latent SIV copies/µg DNA 0.01 - 0.99 1 - 299 300 - 2,999 3,000 - 29,999 > 30,000 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 Neutralizing antibodies direct the killing of SHIV-infected cells *in vitro* 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?





- antiviral defense in newborn macaques, with and without treatment.