

HIV-1-Infected Infants Develop Broadly Neutralizing Antibodies

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Most effective vaccines elicit neutralizing antibodies (NAbs) to prevent infection; however, it is difficult to elicit HIV-1 specific broadly neutralizing antibodies (bNAbs) due to the high antigenic variability of the virus. Furthermore, naturally occurring bNAbs against HIV-1 are uncommon and generally appear relatively late post-infection, suggesting the maturation pathways leading to HIV-1 bNAbs may be complex. Infants infected with HIV-1 generally progress to disease faster than adults, presumably due to an immature and incomplete immune response. However, it is not known whether infants can mount a bNAb response to infection. In a recent paper published in *Nature Medicine*, Drs. Leslie Goo and Julie Overbaugh (Human Biology and Public Health Sciences Divisions) and an international team of collaborators demonstrate for the first time that HIV-1 infected infants can rapidly mount a broad neutralizing antibody response to HIV-1, sometimes within the first year of life.

To determine whether infants infected with HIV-1 mount a bNAb response, the researchers tested the ability of serum from 28 infected infants enrolled in the Nairobi Breastfeeding Trial to neutralize a panel of viruses. More than 70% of these infants had a cross-clade response, meaning they were able to neutralize one or more viruses from a different clade than the virus with which they were infected. Seven infants neutralized viruses across all four clades that were tested. When evaluated longitudinally for neutralization activity, these infants had an initial high titer of NAb that waned within 3 months, consistent with maternally transferred antibody, and then developed a second peak of NAb activity that increased over time, consistent with de novo NAb production.

Both set-point viral load, the stable viral load in a person after acute infection, and HIV envelope-specific antibody levels were strongly correlated with increased breadth of NAb activity in infants (multivariate analysis, $p = 0.02$ and $p = 0.001$, respectively). Except for one infant, there was also a strong correlation between the titer of passively transferred maternal antibodies and the titer of NAbs produced de novo by the infant (Pearson's $r = 0.52$, $P = 0.02$). This result suggests that conserved antigenic features between the maternal and infant virus populations may be shaping the infant de novo NAb response, although additional factors may also play a role. Surprisingly, the researchers could not map infant NAbs to any of the four regions of the HIV-1 envelope protein that are the main targets for adult bNAbs. These results suggest that either infant bNAb responses are polyclonal or that they are targeting a novel epitope, and work in the Overbaugh laboratory is currently addressing this question.

Although infants attain high viral loads, the current study confirms that they do have a competent B cell response and develop bNAbs at least as commonly as adults. This discovery suggests "that future vaccination efforts to induce such antibodies in infants to protect against infection may be feasible. Moreover, HIV-1 infected infants may provide insight into pathways toward the

development of bNAbs within a relatively short time frame as this study raises the possibility that such antibodies may develop more frequently and rapidly in a subset of infants compared to adults," said Dr. Leslie Goo.

[Goo L, Chohan V, Nduati R, Overbaugh J](#). 2014. Early development of broadly neutralizing antibodies in HIV-1-infected infants. *Nature Medicine*. 655-8.

UW/FHCRC Kenya Research Program: Key Collaborating Institutions

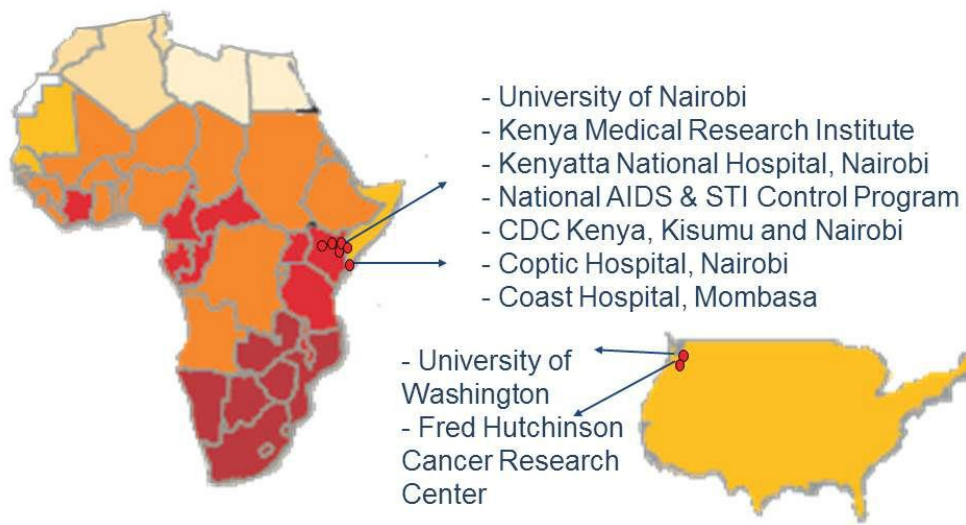


Image from <http://research.fhcrc.org/overbaugh/en.html>

The Nairobi breastfeeding trial is part of a larger international HIV research collaboration, the Kenya Research Program.