# GERMLINE-TARGETING ENV TRIMER ELICITS bNAB PRECURSORS IN INFANT, NOT JUVENILE MONKEYS

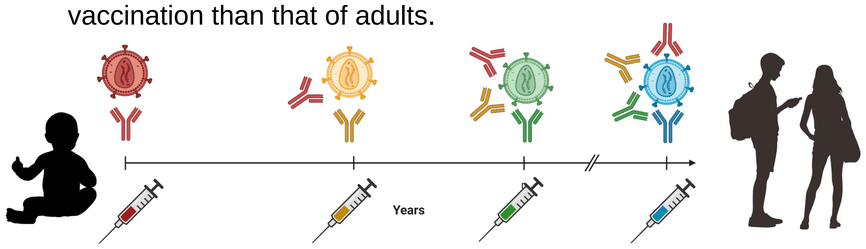
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## INTRODUCTION

- An HIV vaccine that induces protective, broadly-neutralizing antibodies (bnAbs) prior to sexual debut is critical to provide lifelong immunity and prevent the ~410,000 new infections that occur annually among 15-24 yo worldwide.
- Recent work has established that children with HIV develop bnAbs earlier and at a higher frequency than adults, suggesting that the infant immune landscape may be more amenable to the induction of bnAb B cell lineages by vaccination than that of adults.




**Study Goal**

**To assess the ability of bnAb germline-targeting BG505 SOSIP trimers to induce precursor bnAb responses in early life.**

## METHODS

Infant (n=5) and juvenile (n=4) rhesus macaques (RMs) received 3 immunizations of the germline-targeting BG505 GT1.1 SOSIP trimer (50 ug) with the 3M-052-SE adjuvant 6 weeks apart. All RMs were then boosted 12 weeks later with the wildtype BG505.664 SOSIP trimer 3 times in 6-month intervals. Vaccine elicited antibody responses were monitored through 1.5 years.

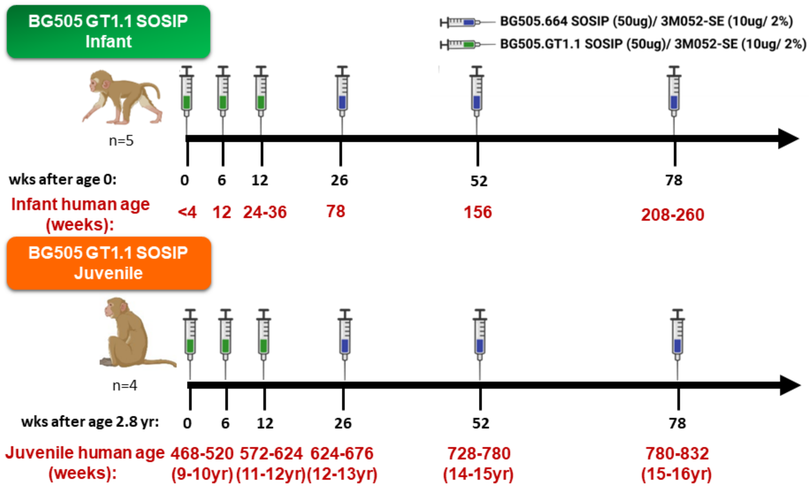



**Figure 1.** Timeline of the BG505 GT1.1 SOSIP (green) and BG505.664 WT SOSIP (blue) immunizations administered to infant and juvenile RMs.

## RESULTS

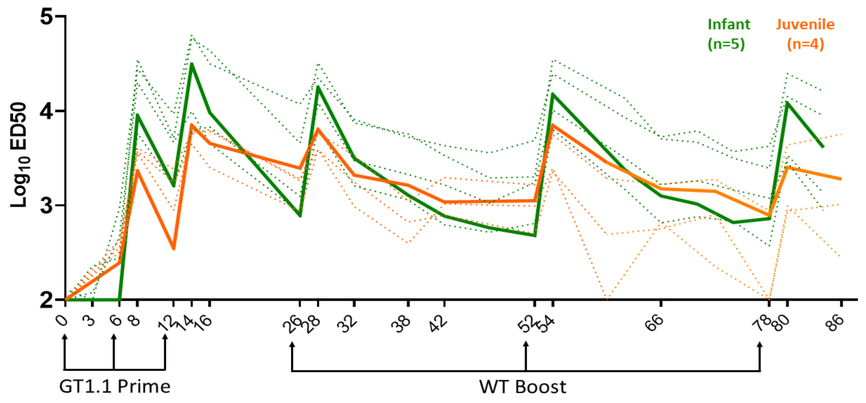



**Figure 2. Juveniles Continue to Display Lower SOSIP GT1.1 Binding Antibodies Compared to Infants Receiving the Same Vaccine Regimen.** Plasma IgG binding responses were measured by ELISA to the GT1.1 immunogen. Both infant RMs and juvenile RMs developed high magnitude IgG binding responses with increased durability following each boosts. Black arrows represent immunization time points.

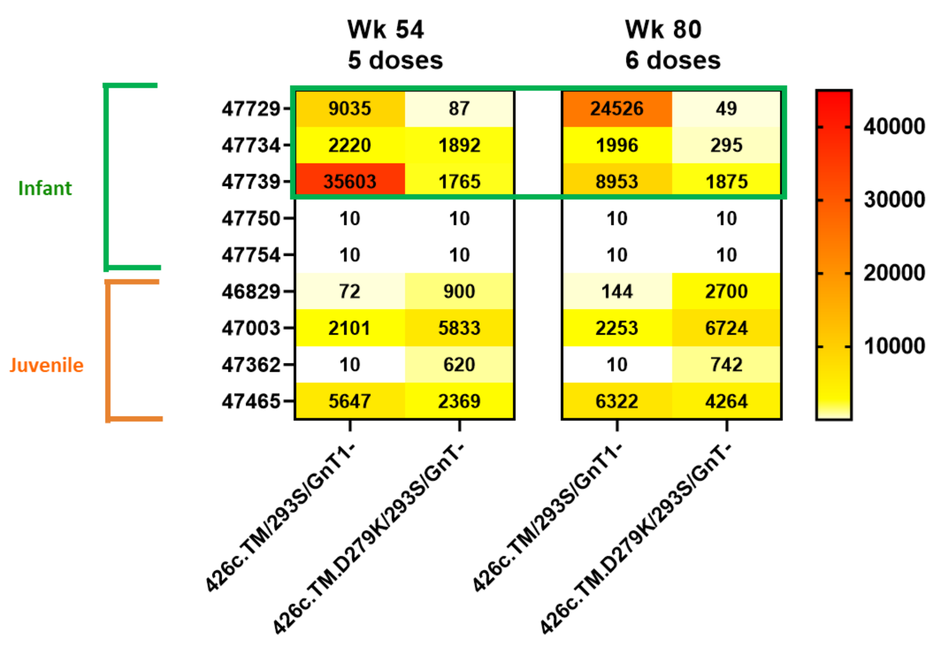



**Figure 3. Three out of Five Infant RMs Developed CD4bs Precursor bNAbs.** Sera was screened at 2 weeks after the 2nd and 3rd immunizations with BG505.664 for the development of VRC01-like CD4-binding site (CD4bs) precursor bnAb responses. Sera at each time point was assayed against the 426c.TM/293S/GnT1- virus, which engages germline-reverted forms of VRC01-class bnAbs, and the CD4bs KO virus, 426c.TM.D279K/293S/GnT-. By wk 80, three GT1.1-immunized infant RMs developed CD4bs precursor bnAb responses (green box).

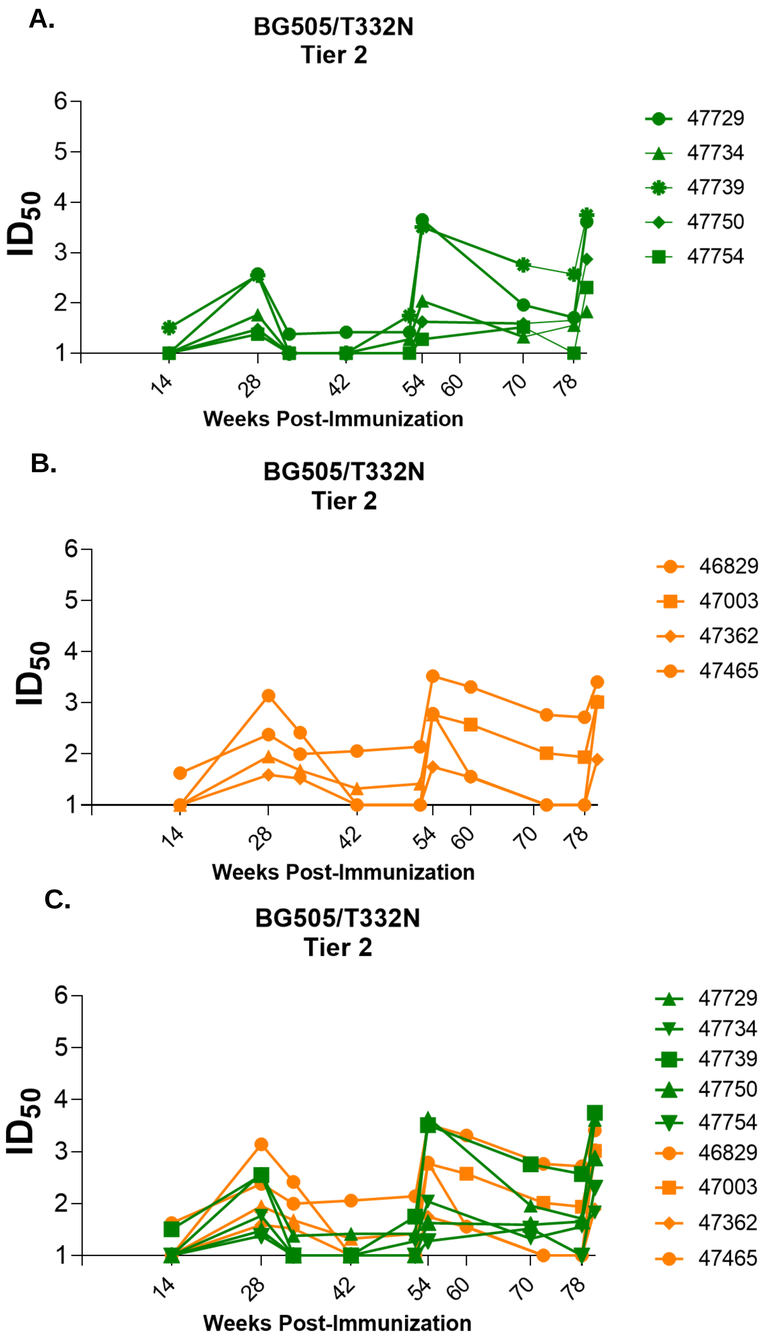



**Figure 4. Infant (A) and Juvenile RMs (B) Both Developed Tier 2 Autologous Virus Neutralization Responses.** HIV-1 neutralization in sera was assayed in TZM-bl cells against BG505/T332N Tier 2 virus. These responses were similar in magnitude across both groups (C).

## CONCLUSIONS

- Durable IgG binding responses were induced in both infant and juvenile RMs, with slightly higher magnitude responses in infants.
- Both infant and juvenile RMs developed Tier 2 autologous virus neutralization responses.
- 3 out of 5 GT1.1 immunized infants developed CD4-binding site targeting bnAb precursor responses

**Our data demonstrates that sequential immunization of infant RMs with germline-targeting and wildtype BG505 SOSIP trimers can induce high serum neutralizing antibody titers and CD4bs bnAb precursors, while these responses were not detectable in vaccinated juvenile RMs. Our results support observations in human studies suggesting that the infant immune environment is better suited for induction of systemic HIV bNAb responses.**

## ACKNOWLEDGEMENTS

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