THE ROLE OF MATERNAL BROADLY NEUTRALIZING ANTIBODY ACTIVITY IN PERINATAL TRANSMISSION OF HIV-1

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BACKGROUND

- Despite increased availability to antiretroviral therapy (ART), up to 5% of women living with HIV (WLH) still transmit HIV-1 to the infant[1].
- Broadly neutralizing antibodies (bNAbs) are the immunologic goal of HIV-1 vaccine candidates; however, in postnatal cohorts, we have reported the presence of bNAbs targeting a single epitope, which contributes to viral escape[3,4].

HYPOTHESIS

WLH with bNAbs against single epitopes of the HIV envelope are at higher risk of perinatal transmission due to viral escape, while multispecific bNAbs could reduce transmission.

METHODS

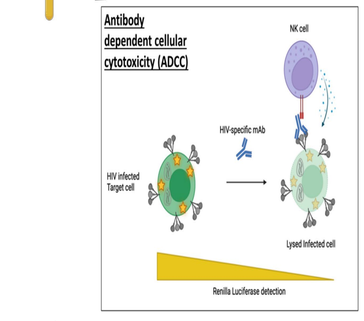
Mother-Infant Cohort Study (MICS)
Pre-ART; enrolled before ART was standard of care
15 Transmitters | 47 Non-Transmitters

NICHD International Site Development Initiative (NISDI) Perinatal
ART administered around delivery for half of enrolled women
6 Transmitters | 23 Non-Transmitters

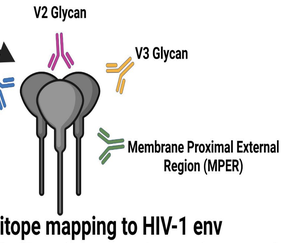
Paired infants with HIV (< 1 year)

Neutralization Screening Strategy

	Virus	Clade
Screen 1	25710	C
	TRO11	B
	X2278	B
	BJOX002000	CRF07
	246F3	AC
Screen 2	X1632	G
	CE1176	C
	CH119	CRF07
	CE0217	C
	CNE55	CRF01



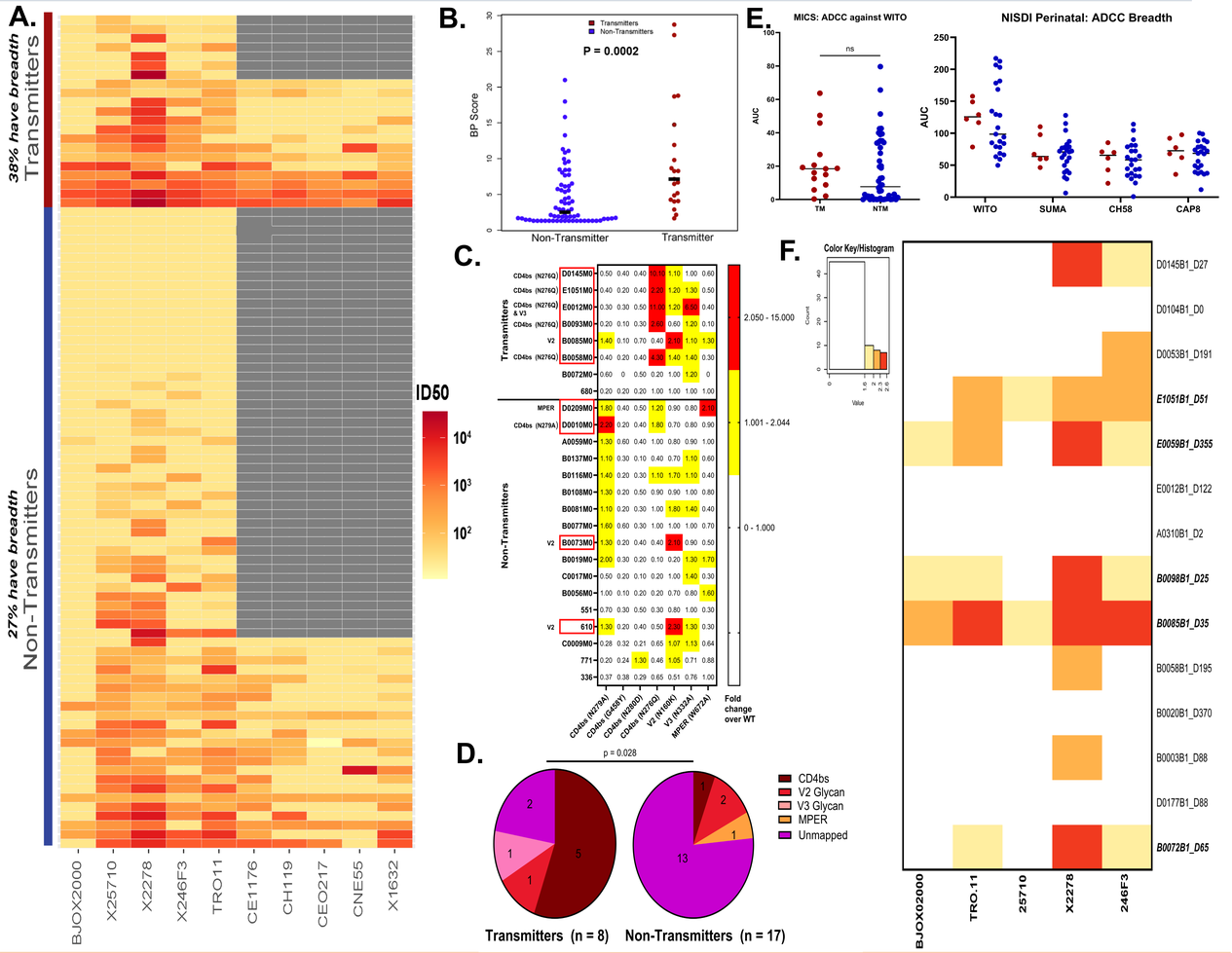
Neutralize ≥ 5 viruses with ID_{50} ≥ 40



bNAb epitope mapping to HIV-1 env
(>2-fold reduction in ID_{50} of mutant viruses for mapping)

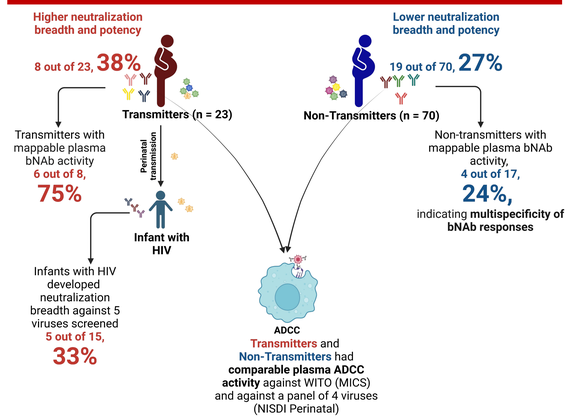
RESULTS

A significantly higher proportion of perinatal transmitters (8 out of 23, 38%) had neutralization breadth and potency compared to non-transmitters (19 out of 70, 27%). 6 out of 8 transmitters (75%) had mappable bNAb activity, while the majority of non-transmitters remain unmapped (24% mapped).



A. **Plasma neutralizing antibody breadth** in transmitters (n = 21) and non-transmitters (n = 70) was measured against a global panel of 10 viruses. Grey indicates neutralization was not assessed. **B.** Transmitters had significantly higher breadth-potency scores[3] (p=0.0002) **C. Epitope mapping** was assessed in **8 transmitters and 17 non-transmitters** against CD4bs, V2, V3 Glycan, and the membrane proximal external region (MPER) of HIV-1 env. Mapped participants boxed in red and indicates the mapped epitope. **D.** Significantly more transmitters could be **mapped to an epitope** (p = 0.028, two-tailed Fisher's exact test). **E. ADCC against WITO** was assessed for MICS, and **ADCC breadth** was assessed against 4 viruses for NISDI. **F. Neutralization breadth** was compared for **paired infants** of transmitters from the MICS cohort against Screen 1 viruses; IDs with breadth represented in ***bold italic***.

CONCLUSIONS



- Increased bNAb activity in transmitters is often mappable to a single epitope, which could lead to viral escape and perinatal transmission.
- ADCC was similar between transmitters and non-transmitters.
- A third of infants with perinatal HIV acquire breadth within the first year of birth.
- bNAb-based pediatric HIV prevention and treatments that are synergistic with ART will likely need to be multi-specific to effectively eliminate and cure pediatric HIV.

FUTURE DIRECTIONS

- Map bNAb responses for infants with HIV.
- Sequence *env* variants from transmitter-infant pairs using single genome amplification (SGA).
- Generate Env pseudoviruses from maternal and T/F infant pairs to measure susceptibility to neutralization by autologous plasma.[5]

ACKNOWLEDGEMENTS

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