PRESENCE OF CXCR4-USING HIV-1 VIRUS IN NEWLY DIAGNOSED INDIVIDUALS IN NORTH CAROLINA

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BACKGROUND

HIV-1 uses either CCR5 or CXCR4 as the coreceptor to enter host cells. Transmitted viruses are usually CCR5-using (R5 virus), and CXCR4-using (X4/dual) viruses emerge in the late stage of disease. In 2018 we implemented a statewide recency assay for HIV-positive tests conducted at the NC public health lab. This platform uses a UMI-based NGS approach to sequence portions of the HIV-1 genome including the env gene V3 region for co-receptor prediction. We assessed the prevalence of X4 viruses among people with newly diagnosed HIV-1 from 2018 to 2021.

METHODS

- Remnant diagnostic sera from people with new HIV-1 diagnoses were sequenced using the Multiplexed Primer ID MiSeq protocol targeting the HIV-1 pol gene and env V1-V3 region.
- Recent HIV-1 infections (within 9 months of infection) were estimated based on pairwise sequence diversity.
- Coreceptor tropism was predicted using Geno2Pheno algorithm using two false positive rate (FPR) cut-offs of 2% and 5.75%.

	Recent (N=288)	Chronic (N=340)	Indeterminant (N=98)	Total (N=726)	p value
X4/Dual virus 2% FPR cut-off	17 (5.9%)	47 (13.8%)	11 (11.2%)	75 (10.3%)	0.005
X4/Dual virus 5.75% FPR cut-off	45 (15.6%)	91 (26.8%)	20 (20.4%)	156 (21.5%)	0.003

Table 1. X4 viruses predicted in the study cohort stratified by recency status

The overall transmission of HIV-1 X4 viruses is approx. 10%, significantly higher than previously thought.

RESULTS

- A total of 726 people had sufficient sequence depth for the analysis.
- Overall, using the 2% and 5.75% cutoffs, we found that 10.3% and 21.5% had X4 variants, with a median abundance within the individual viral populations of 32.3% (IQR: 10.9-85.2%) and 53.3% (IQR: 11.5-97.6%), respectively.
- Using the 9-months recency cut-off, we found significantly more X4 variants in the chronically infected individuals (13.8 and 26.8%) than the recently infected (5.9 and 15.6%) using both FPR cut-offs ($p<0.01$). See in **Table 1**.

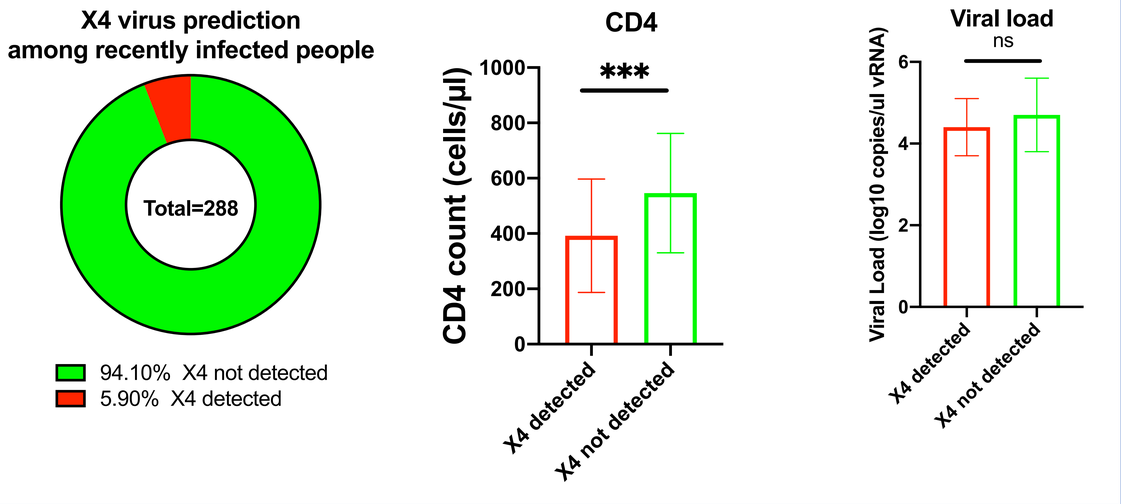


Figure 1. CD4 cell count and viral load of recently infected individuals with X4/dual viruses using 2% FPR cut-off.

RESULTS, cont.

- Among the recently infected patients, those with X4 variants had significantly lower CD4 counts using 2% FPR cut-off ($p<0.01$). See in **Figure 1**.
- Most of the X4 variants found in the recent infections had homogenous populations, with a median abundance greater than 95% at both cut-offs, suggesting they were transmitted X4 variants. Conversely, most chronically infected individuals had mixed populations of R5 and X4 viruses, consistent with a late diagnosis of infection. See in **Figure 2**.
- Carrying X4 variants was not associated with having significantly more DRMs at the pol region.

CONCLUSIONS

- We previously observed that viruses with an FPR≤2% have an X4 entry phenotype while half of those with an FPR from 2% to 5.75% have an X4 entry phenotype. Thus, we estimate that the overall transmission rate of X4 viruses is approx. 10%. This is significantly higher than previously thought and may represent further maturation of the epidemic with an increased fraction of transmissions from chronically infected people not on therapy.

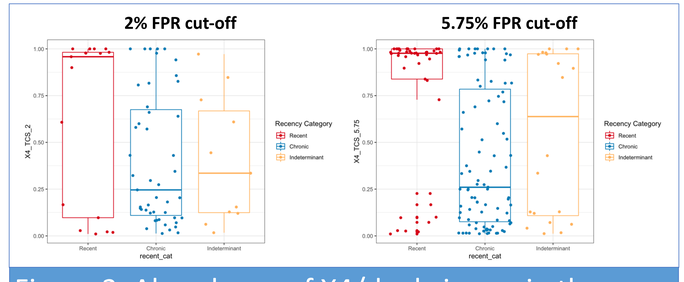


Figure 2. Abundance of X4/dual viruses in the individual viral populations by recency status. Two FPR cut-offs were applied in this analysis.

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