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## BACKGROUND

HIV-1 envelope (env)-specific broadly neutralizing antibodies (bNAbs) have several potential clinical benefits over current antiretroviral treatment (ART) options. The bNAbs with modified Leucine-Serine (LS) Fc receptors permit infrequent subcutaneous dosing and may facilitate viral reservoir reduction and contribute to functional cure. However, data on HIV-1 Env evolution and bNAb susceptibility in perinatally infected infants are limited.

## METHODS

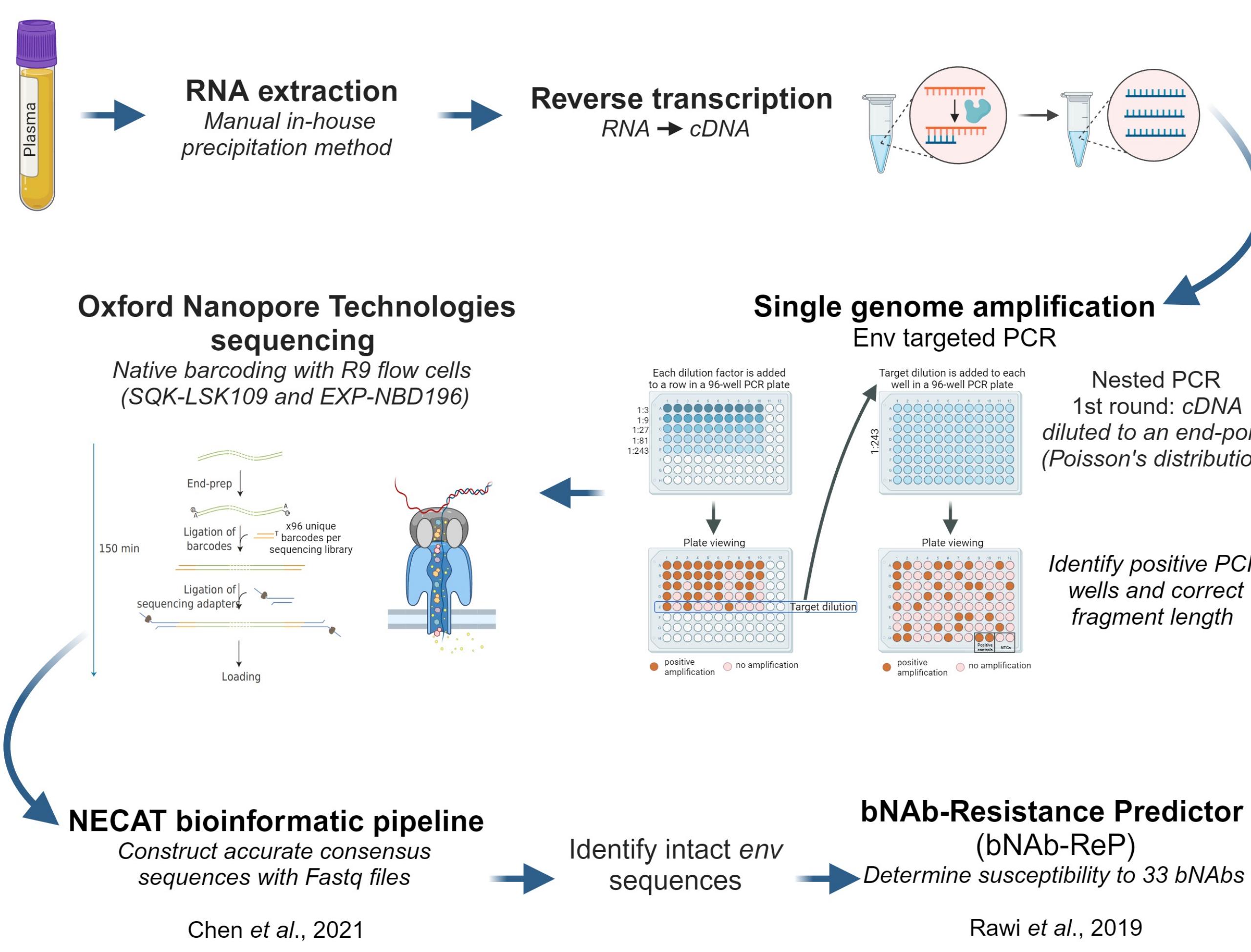
### Study population:

- Five infants (4 female) living with HIV-1 with intermittent viraemia
- Initiated 3TC, LPV/r & ABC within 90 days of diagnosis
- Investigated over 19.3 months (range: 16.9 - 21)

Table 1. Patient samples investigated and the respective viral loads (copies/mL)

Patient identifier	Visit 2 2 months	Visit 3 3 months	Visit 4 6 months	Visit 5 12 months	Visit 6 18 months	Visit 7 24 months
SA-TY-012	355 930	902 552	1 344 319	81 796	653 059	333 199
SA-TY-015	293 787	-	200 345	738	-	115
SA-TY-025	3 382	391 854	19 376	135 969	200	4 143
SA-TY-032	1 150	754	154	<100	LDL	8 885
SA-TY-034	1 049	428 562	9 650	1 954	9 239	1 420

Plasma sample investigated



Chen et al., 2021

Rawi et al., 2019

Early intra-patient env evolution and diversification seems to have a limited impact on bNAb susceptibility, whereas predicted bNAb susceptibility varied across individuals due to a high level of inter-patient env diversity

## RESULTS

The intra-patient average pairwise distances (APD) ranged from 0.08% - 1.29% (median: 0.43%). Different evolutionary patterns were observed, and length variation emerged in 4/5 (80%) infants. Phylogenetic trees showed temporal structure in four cases with new variants emerging either from majority or minority populations or apparent ancestral or archived variants. All variants were identified as CCR5-tropic by three genotypic prediction models.

Table 2. Investigation of HIV-1 Env of five infants and the highest predicted bNAb susceptibility

Patient	Duration of observation (months)	Env APD# (%)	Length variation (base pairs)
SA-TY-012	16.9	1.02	2 550 – 2 571
SA-TY-015	19.5	0.08	2 568
SA-TY-025	19.1	0.36	2 565 – 2 568
SA-TY-032	19.3	1.29	2 568 – 2 583
SA-TY-034	21	0.43	2 553 – 2 568

# APD – average pairwise distance

Overall, the predicted bNAb susceptibility showed a higher inter-patient than intra-patient variability.

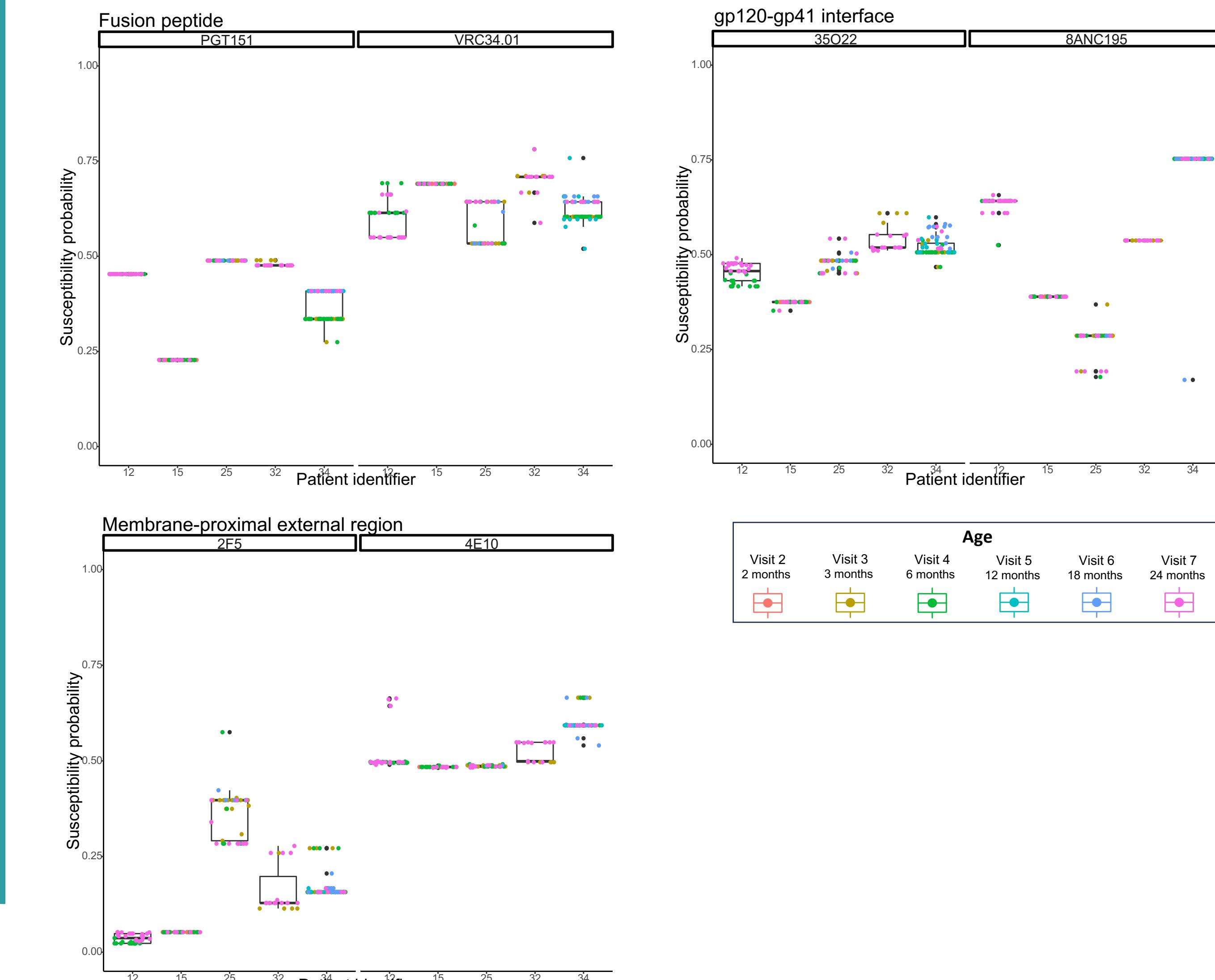
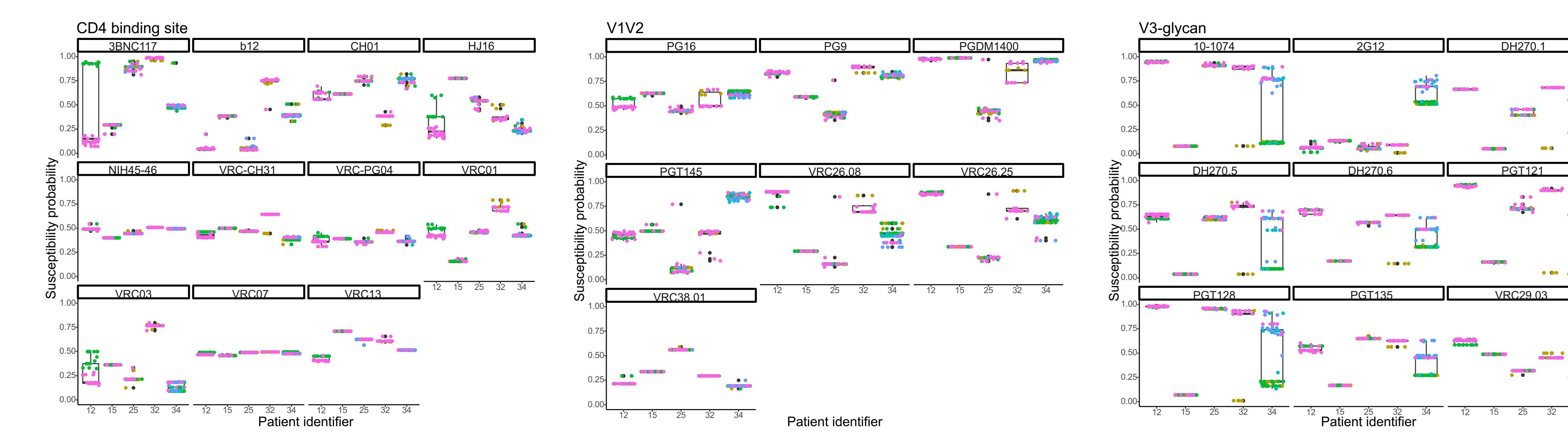


Figure 2. The bNAb-ReP predicted susceptibility results for each binding domain

## CONCLUSIONS

We developed an efficient env genotypic assay, combining single-genome sequencing with ONT to accommodate env sequence length variation as phenotypic bNAb susceptibility testing is costly and has low reproducibility. Applying our workflow, the predicted susceptibility to bNAbs varied across individuals due to high levels of inter-patient env diversity. Early ART-treated infants often have viraemia due to adherence challenges. However, early intra-patient env evolution was limited and unlikely to impact bNAb susceptibility. Updated prediction algorithms require validation across HIV-1 subtypes.

## ADDITIONAL KEY INFORMATION

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