HIGH PREDICTED bNAb RESISTANCE AMONG ADULTS WITH HIV-1 SEROCONVERSION IN BOTSWANA

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BACKGROUND

- We used proviral HIV-1C sequences from adults with documented HIV-1 seroconversion in Botswana to determine HIV drug resistance mutations and predict (in silico) resistance to 33 known broadly neutralizing antibodies (bNAbs).

METHODS

- We analyzed proviral sequences from adults with documented HIV-1 seroconversion (N=140) from a population-based household study (Botswana Combination Prevention Project, 2013-2018).
- HIV-1C near-full length proviral sequences were generated and adjusted for hypermutations using Hypermut.
- Surveillance drug resistance mutations (SDRMs) associated with protease inhibitors (PI), integrase strand transfer inhibitors (INSTI), nucleoside reverse transcriptase inhibitors (NRTI) and non-nucleoside reverse transcriptase inhibitors (NNRTI) were analyzed according to Stanford CPR tool.
- HIV gp120 region was used to predict sensitivity of contact sites to 33 known bNAbs using the bNAb-ReP algorithm (https://github.com/RedaRawi/bNAb-ReP).
- All gp120 alignments were also used to determine the number of potential N-linked glycosylation sites (PNGS) and compared among bNAb resistant and sensitive strains.

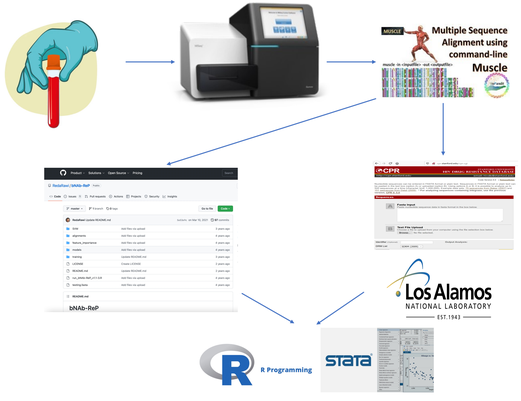


Fig 1: Specimen testing and data analysis schema

We report low levels of SDRMs but high prevalence of predicted bNAb resistance in adults with HIV seroconversion in Botswana.

RESULTS

- **One-hundred-and six (76%) seroconverters were ART-naïve at the time of sample collection with a median viral load of 3.9 (Q1, Q3: 3.2,4.4) log10 copies/mL.**
- **Median age was 27 years (Q1, Q3: 22,33) and most (79%) were female.**
- **The overall prevalence of any SDRMs at baseline was 6.6%. We found PI-, NRTI-, NNRTI- and INSTI-associated SDRMs in 1.9% (95%CI 0.2–6.6), 3.8% (95%CI 1.0–9.4), 1.9% (95%CI 0.2–6.6), 1.9% (95%CI 0.2–6.6), respectively.**
- **Prevalence of predicted resistance to 1 or more bNAbs was high among seroconverters (Fig 2)**
- **100% of sequences showed resistance to 2F5, PG16, PGT151 and VRC34.01. In contrast, most sequences (>60%) were likely susceptible to 10-1074, PGDM1400, PCT128, VRC13 and VRC25.25.**
- **No difference was observed in the frequency of PNGS compared to bNAb resistance/sensitivity**

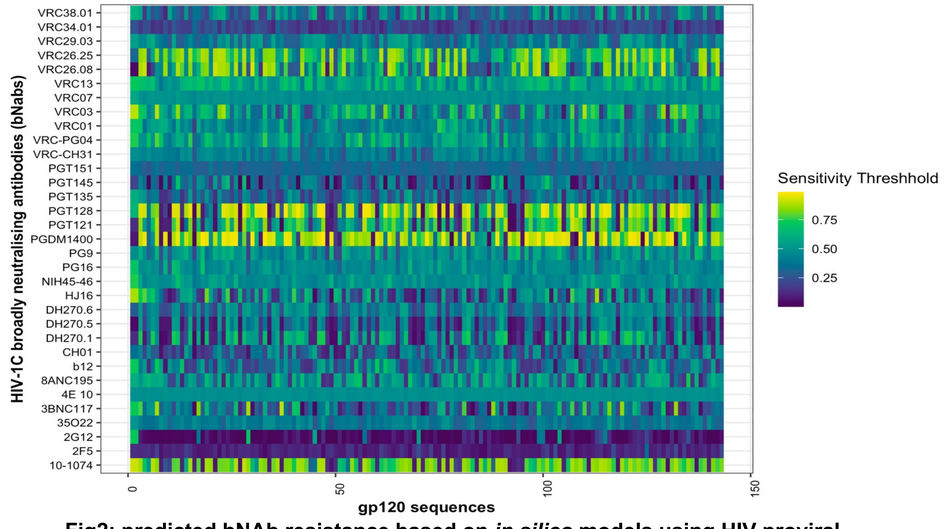


Fig2: predicted bNAb resistance based on *in silico* models using HIV proviral sequences from seroconverters in Botswana

CONCLUSIONS

- This is the first study to use machine learning to determine bNab neutralizing capacity in Botswana
- We report low levels of HIV drug resistance mutations in adults with HIV seroconversion in Botswana
- We report high prevalence of predicted bNAb resistance in adults with HIV seroconversion in Botswana reflecting that very few bNabs could potentially block the current circulating viral strains within country
- Our finding warrant further investigation of bNAbs that would work as clinical immunotherapies in Botswana
- Our finding also warrant further investigation of bNAb isolates prodced within the Botswana setting.

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