



# Investigating HIV Molecular Epidemiology and Drug Resistance In Ghana

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**Study background and objective:** HIV genetic diversity is highest in West/Central Africa due to the pandemic's origins in this region, but this diversity remains understudied. **Here, we characterize HIV subtype diversity, drug resistance and predicted coreceptor usage in Ghana.**





## BACKGROUND

- The most prevalent HIV-1 strain in Ghana, West Africa, is the circulating recombinant form CRF02\_AG. Subtype G, subtype A and various complex recombinants are also present.
- To date however, only 31 full-genome HIV-1 sequences have been published from Ghana, all from 2003 or earlier.
- Recent ART resistance data based on WHO guidelines is lacking in Ghana, as is information on coreceptor usage

## METHODS

- Cross sectional study with 103 participants recruited.
- Bulk nested RT-PCR performed on plasma HIV RNA, followed by Sanger and Illumina sequencing
- Recombinant Identification Program (RIP) used for subtyping.
- HIV polymerase region interpreted for drug resistance using the Stanford HIV database.
- Coreceptor usage data inferred from envelope-V3 region using geno2pheno (g2p) algorithm.

## PARTICIPANT CHARACTERISTICS

<b>Sex at birth</b>	<b>n=96</b>
Male, n (%)	47 (49%)
Female, n (%)	49 (51%)
<b>Age in years</b>	<b>n=96</b>
Males, median [IQR]	41 [32-48]
Females, median [IQR]	36 [29-51]
<b>Plasma viral load</b>	<b>n=27</b>
median [IQR] x 10 <sup>3</sup> copies/ml	188 [38-747]
<b>ART Status</b>	<b>n=92</b>
ART Naïve, n (%)	82 (89%)
Previously Treated, n (%)	10 (11%)
<b>Infection risk group</b>	<b>n=96</b>
Heterosexual, n (%)	81 (84.4%)
MSM, n (%)	1 (1%)
Vertical Transmission, n (%)	1 (1%)
Sharps/Needles, n (%)	4 (4.2%)
Unknown/Unsure, n (%)	9 (9.4%)

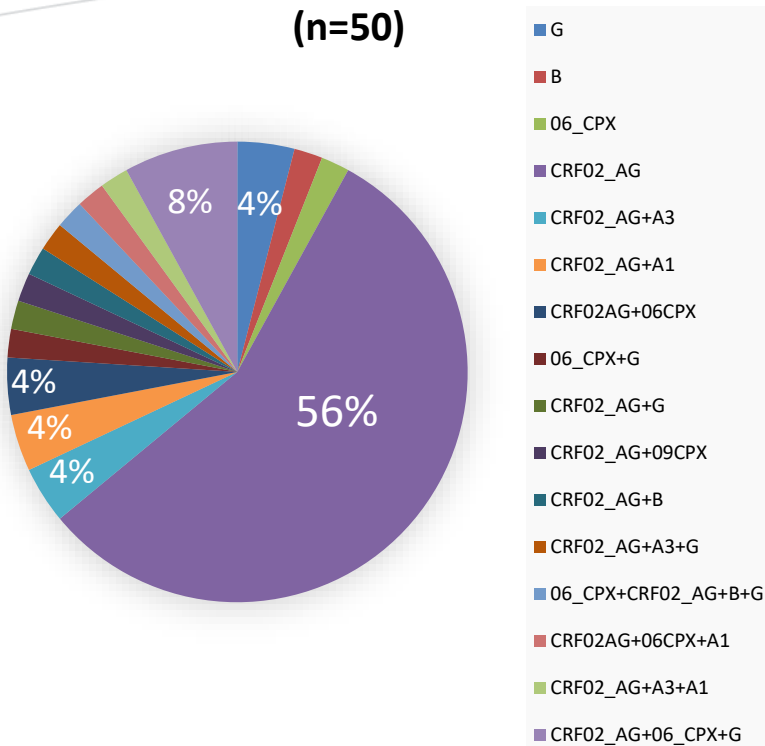
Table reports available data to date, obtained by participant self report and treatment records.



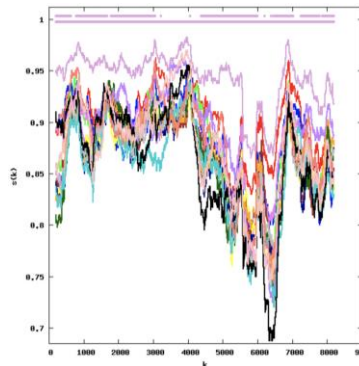
# HIV SUBTYPE DIVERSITY

## WHOLE GENOME HIV SUBTYPING

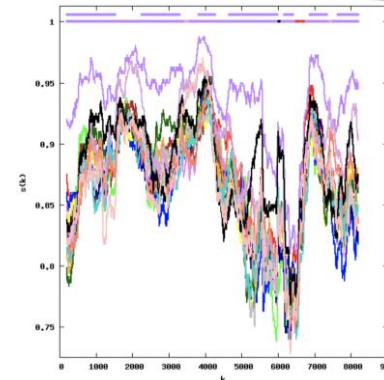
(n=50)



### Example CRF02\_AG

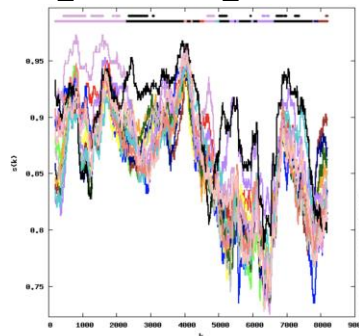


### Example subtype G



### Example complex recombinant

#### 06\_CPX+CRF02\_AG+B+G



### Legend

- CONSENSUS\_A1
- CONSENSUS\_A2
- A3\_SN\_01\_DDI579
- CONSENSUS\_A6
- CONSENSUS\_B
- CONSENSUS\_C
- CONSENSUS\_D
- CONSENSUS\_F1
- CONSENSUS\_F2
- CONSENSUS\_G
- CONSENSUS\_H
- CONSENSUS\_J
- CONSENSUS\_01\_AE
- CONSENSUS\_02\_AG
- 06\_cpx\_AU\_96\_BFP98
- 09\_cpx\_GH\_96\_96GH291

Figures 2-4: Examples of subtyping results for individual full-genome HIV sequences.

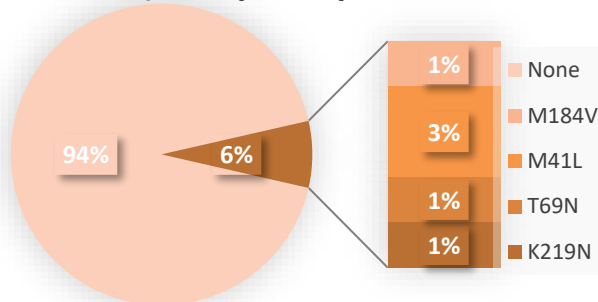
RIP similarity plots are shown. A confidence interval of 0.95 and window size of 400 were used. The two bars at the top of each plot indicate the best match (lower bar) and associated statistical significance (upper bar). Legend at lower right.

Fig 1: Cohort subtype distribution, determined from full-genome HIV sequences. Categories indicate subtype composition, not necessarily shared breakpoints.

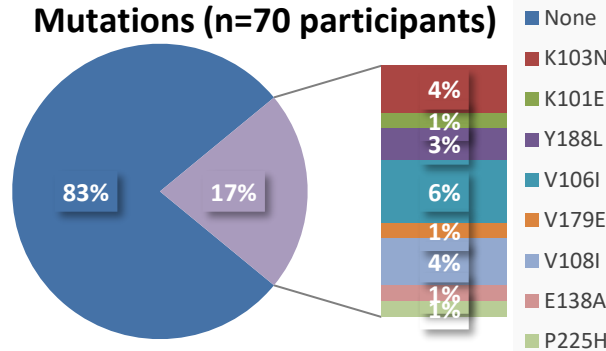


# DRUG RESISTANCE

**Fig 5: NRTI Resistance Mutations (n=70 participants)**



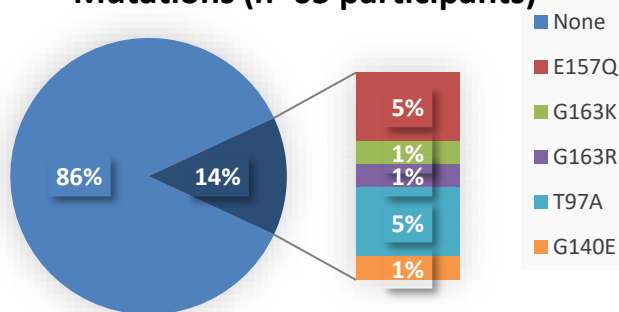
**Fig 6: NNRTI Resistance Mutations (n=70 participants)**



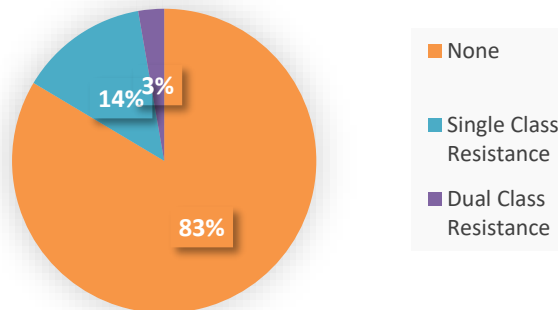
**Fig 5-7: Prevalence of NRTI, NNRTI and Integrase Inhibitor-associated resistance mutations.**

- No resistance to protease inhibitors was observed.
- All resistance-associated mutations are reported here, regardless of Stanford HIVdb score.
- Percentages (%) reported in insets may not add up to the total, due to rounding and/or >1 mutations/participant
- NNRTI-associated resistance mutations were the most prevalent overall.

**Fig 7: Integrase Resistance Mutations (n=65 participants)**



**Fig 8: Overall Level of Resistance (n= 73 participants)**

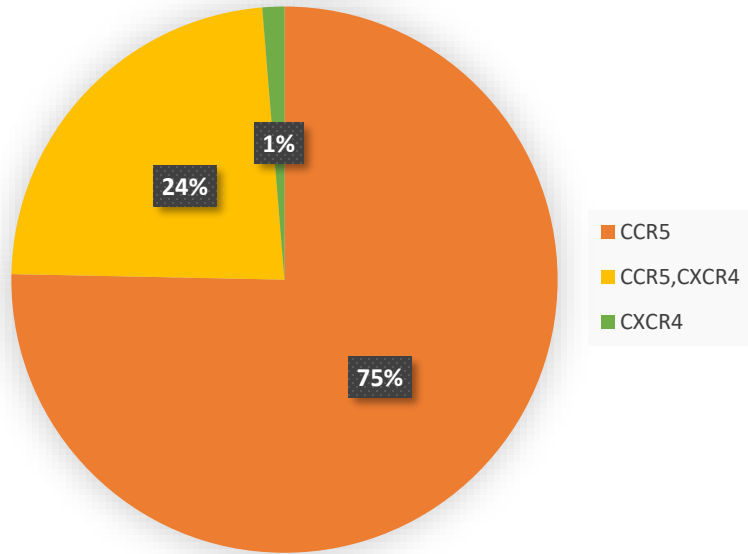


**Fig 8: Overall level of resistance, by drug class.**

- The resistance threshold was defined as a Stanford HIVdb score of 3 or higher for at least one drug in the class.
- Of the 10 individuals with single class drug resistance, 8 had NNRTI resistance, 1 had NRTI resistance and 1 had Integrase inhibitor resistance.
- The two cases of dual-class resistance were NRTI/NNRTI and NRTI/Integrase inhibitors, respectively.
- 16% of ARV-naïve individuals harbored drug resistance, with NNRTI resistance representing the most common type.



## INFERRED CORECEPTOR USAGE (n=77)



**Fig 9: Inferred Co-receptor usage of Ghanaian HIV strains.**

Results are based on analysis of Illumina sequencing of the HIV envelope region, where V3 loop sequences were interpreted using the g2p Algorithm.

The majority (75%) of the cohort harbored HIV that used the CCR5 receptor exclusively.

A considerable minority (24%) harbored mixed populations of CCR5-using and CXCR4-using HIV. For these individuals, CXCR4-using populations were present at a median of 15% of the overall viral population.

One participant was found to have exclusively CXCR4-using HIV.

## CONCLUSIONS

- Results confirm CRF02\_AG as the most prevalent HIV strain in Ghana, but unique and complex HIV recombinants also circulate.
- 16% of ARV-naïve individuals harbored drug resistance mutations, with NNRTI resistance representing the most common type.
- CCR5-using strains predominate.