HIV-1 Phylodynamics and Phylogeography among High-Risk and General Populations in Uganda

Gonzalo Yebra[1], Manon Ragonnet-Cronin[1], Deogratius Ssemwanga[2], Chris M. Parry[2], Christopher Logue[3], Patricia A. Cane[3], Pontiano Kaleebu[2] and Andrew J. Leigh Brown[1]

[1]Institute for Evolutionary Biology, University of Edinburgh, Edinburgh, UK; [2]MRC/UVRI, Uganda Research Unit on AIDS, Entebbe, Uganda; [3]Public Health England, Porton, UK.

CONTACT:
gonzalo.yebra@ed.ac.uk
http://hiv.bio.ed.ac.uk/

BACKGROUND

Uganda presents an HIV prevalence of 7% in adult population[1]), but it is much higher in high-risk groups: 37% in female sex workers (FSW)[2] and 22% in fishing communities around Lake Victoria[3].

We reconstruct the history and spread of HIV subtypes A1 and D in Uganda, and transmission dynamics of some high-risk communities and general population.

METHODS

We analysed 162 HIV *pol* sequences from 3 populations sampled between 2005-2010 (**Fig. 1**):

- FSW based in Kampala (n=42)
- Lake Victoria fisher-folk communities (n=46)
- A rural clinical cohort (RCC) in Masaka, SW Uganda (n=74).

We added Ugandan sequences from GenBank (177 A1; 235 D) with sampling city (Kampala, Entebbe and Rakai) and date (1992-2005).

We discarded recombinants (using SCUEAL[4]) and sequences with high mutation rates (using Path-O-Gen[5]). Clusters were defined by statistical support (>90%) and genetic distance (<4.5%) using ClusterPicker v1.3[6].

We reconstructed the evolutionary history of subtypes A1 and D in Uganda, including 8 D and 3 A1 sequences from 1986 to calibrate the molecular clock; and assessed mobility of HIV within Uganda applying a discrete traits analysis (BSSVS) using BEAST 1.7[7].

REFERENCES

1. UNAIDS 2010 Report (http://www.unaids.org/).
2. Vandepitte et al. Sex Transm Dis. 2011; 38:316.
3. Asiki et al. Sex Transm Infect. 2011; 87:511.
4. Kosakovsky Pond et al. PLoS Computational Biology 2009; 5: e1000581 (http://www.datamonkey.org/).
5. Path-O-Gen: http://tree.bio.ed.ac.uk/software/pathogen/.
6. Ragonnet-Cronin et al. BMC Bioinformatics 2013; 14:317 (http://hiv.bio.ed.ac.uk/software.html).
7. Drummond AJ et al. Mol Biol Evol 2012; 29: 1969 (http://beast.bio.ed.ac.uk/).

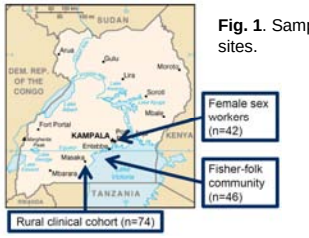


Fig. 1. Sampling sites.

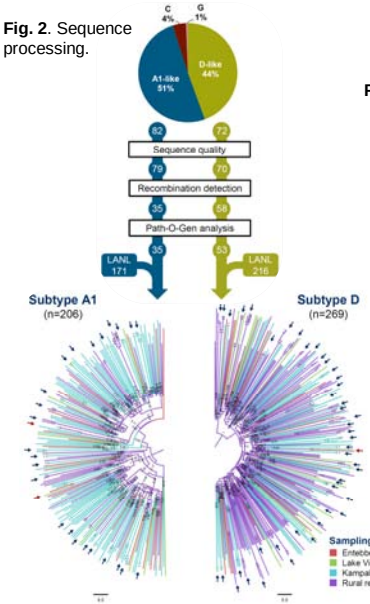


Fig. 2. Sequence processing.

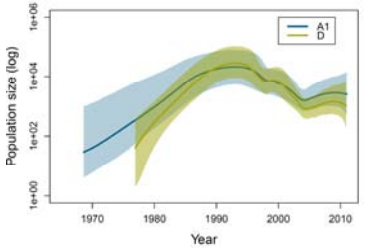


Fig. 5. Bayesian Skyride plot showing the change in the viral population size across time.



Fig. 6. HIV spread in Uganda. Numbers indicate sequential order of the movements.

Fig. 3. Bayesian trees. Arrows denote clusters (red arrows indicate clusters involving different populations).

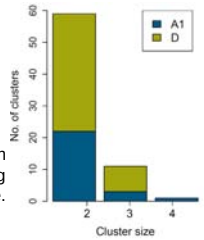


Fig. 4. Transmission networks according to size and subtype.

RESULTS

Subtype distribution: 82 (50.6%) A1-like, 72 (44.4%) D-like, 7 (4.3%) C and 1 (0.6%) G (**Fig. 2**); 44 A1-like and 12 D-like were recombinants. A1 dominant (60.7%) in the cities (Kampala, Entebbe) and D (74.6%) in the rural areas (Rakai, Masaka).

Transmission groups: 71 (26 A1, 45 D) (**Fig. 3**), mostly pairs (59, 83.1%) (**Fig. 4**); and only 3 (4.2%) involving different populations.

A third (32.6%) of sequences were clustered (27.7% for A1; 36.4% for D), including almost half (45.2%) of RCC sequences while fishermen (23.1%) and FSW (5%) were more interspersed in the trees.

Rural samples clustered more than urban (Kampala, Entebbe) (39.4% vs. 27.5%, P=0.01).

A1 and D phylodynamics: most recent common ancestors in 1959.6 for A1 and 1973.4 for D. Both subtypes (**Fig. 5**) grew exponentially in the 1970s-1980s and decreased in the 1990s. An increase from 2005 could predict a rise in HIV prevalence.

Subtypes A1 and D phylogeography: both originated in the rural, southwest Uganda (Masaka, Rakai) with subsequent spread from Kampala to Entebbe and Lake Victoria (**Fig. 6**).

CONCLUSIONS

Subtype A1 in Uganda is older than subtype D, emerging in the late 1950s and early 1970s, respectively.

Of the regions studied, the south western rural areas are the probable origin of the Ugandan HIV epidemic.

Sequences from rural areas clustered more frequently while fishermen and sex workers were more interspersed in the trees. We found little intermixing between these 3 populations.

ACKNOWLEDGMENTS

We thank the study populations, the MRC/UVRI staff and Nicola Cook (PHE, Porton). Work in Uganda was funded in part by MRC-UK, DFID-UK and EDCTP. GY was supported by funds from the ICONIC project.