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

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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].

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.

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