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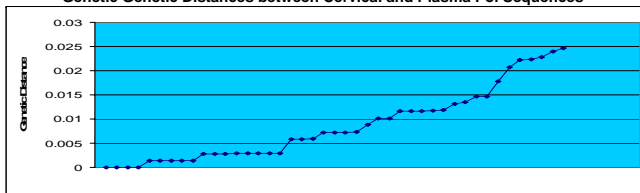


I. Background and Objectives

- HIV-1 from genital secretions (GS) and plasma may infect infants during gestation or delivery.
- HIV-1 in GS and plasma may differ with respect to drug resistance, immune escape mutation(s) and envelope tropism.
- Phylogenetic comparison of genital tract and plasma virus among pregnant, HIV-infected women may identify compartmental differences and sequence variation in potentially transmissible subtype C HIV-1.
- We examined the reverse transcriptase (RT) region of *pol* and *env* in genital (cervical) and plasma samples from subtype C HIV-1 infected women

II. Methods

- HIV-infected pregnant women attending antenatal clinics in Zimbabwe were enrolled between January 1999 and June 2001.
- Cervical and plasma samples were collected at 36 weeks gestation, before short-course AZT was initiated.
- Population sequences were generated from genital and plasma samples for *pol*, and the RT sequence, amino acids 1 to 238, was analyzed from 43 paired samples.
- The general time reversible model used to determine genetic distances (PAUP).
- ~20 distinct *env* clones were obtained by TA cloning from GS and plasma of 6 transmitting mothers to assess compartmental diversity and tropism.
- Env* tropism was estimated by a subtype C specific X4 algorithm (PSSM)

Figure 2
Genetic Genetic Distances between Cervical and Plasma Pol Sequences

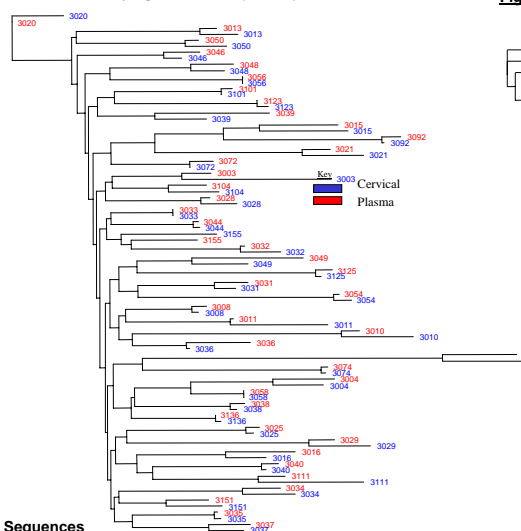
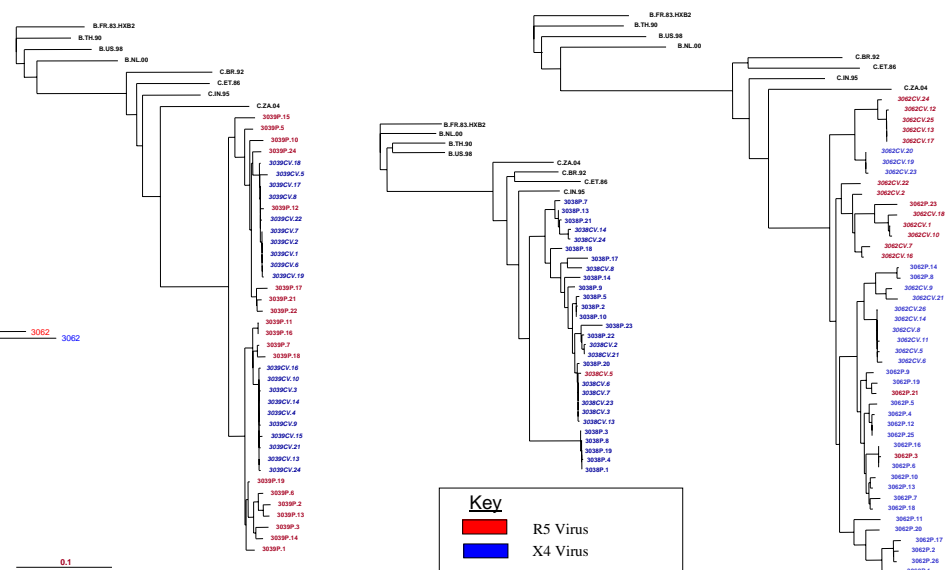
Red circles indicate the genetic distances among women who transmitted HIV to their infant.

Table 1
Baseline characteristics of 43 women in whom cervical and plasma sequence was obtained

	Overall (n=43)	Transmitters (n=7)	Non-Transmitters (n=36)	P-value*
CD4 per cu mm (Range:25%-75% IQR)	310 (11-1055; 196-532.5)	280 (189-253; 265-474)	317 (11-1055; 184-567)	0.72
Plasma VL log ₁₀ copies/ ml (Range:25%-75% IQR)	4.24 (2.5-5.75; 3.52-4.8)	4.46 (2.65-4.03; 3.26-5.33)	4.24 (2.50-5.63; 3.52-4.52)	0.76
Cervical VL log ₁₀ copies/ ml (Range:25%-75% IQR)	3.55 (2.29-5.63; 3.06-4.09)	3.55 (2.65-4.03; 3.13-3.55)	3.61 (2.29-5.63; 3.02-4.31)	0.57
HPV Positive - proportion	33/43 (77%)	5/7 (71%)	28/36 (78%)	0.29
Genetic Distance (Range:25%-75% IQR)	0.007 (0-0.025; 0.003-0.013)	0.021 (0-0.024; 0.003-0.024)	0.007 (0-0.023; 0.003-0.012)	0.086

Data are median unless otherwise indicate

*P-values calculated using the Chi-Square Test for Categorical Variables and the Wilcoxon Rank-Sum Test for Non-parametric Continuous Values

Figure 1
Phylogenetic Tree: *pol* sequences**Figure 2**
Phylogenetic Tree: *Env* sequences showing the phylogenetic relationship between R5 and X4 clones

III. Results

- The median genetic distance in *pol* was 0.047 for cervical sequences (range: 0.021- 0.105) and 0.044 for all plasma sequences (range: 0.019-0.093).
- The median genetic distance within paired cervical and plasma sequences was 0.007 (range: 0- 0.025) – see Figure 1
- There was a trend of greater genetic distance between samples from women who transmitted to their babies compared to those who did not ($p=0.086$, Wilcoxon Rank-Sum Test).
- 1 transmitting woman had pure R5 virus that was subtype B in *env* (confirmed by RIP), but subtype C in the *pol* region of RT
- 3/6 transmitting women had evidence for both R5 and X4 virus by clonal analysis. The proportion of X4 and R5 viruses in the GS and plasma differed, and also segregated in variable patterns as shown in the phylogenetic trees in Figure 2.
- Two women had a variable mix of R5 and X4 virus in both plasma and genital secretions
- One woman had evidence for X4 virus in genital secretions but not in plasma
- Three had only R5 viruses in both genital secretions and plasma (not shown)

IV. Summary and Conclusions

- Among subtype C HIV-1 infected pregnant women, selection of viruses in genital secretions relative to plasma, in both *pol* and *env* genes, provide evidence for independent compartmental replication.
- Tropism in plasma virus may not reflect tropism of HIV compartmentalized in genital secretions.
- Frequent identification of X4 virus in genital secretions and plasma of women who transmitted HIV to their infants suggests that further studies of tropism of virus isolated from genital secretions are warranted as R5 inhibitors are developed for pre and post-exposure prophylaxis and prevention.