Transmission, Variation, and Evolution of In Utero Transmitted HIV-1

#0781

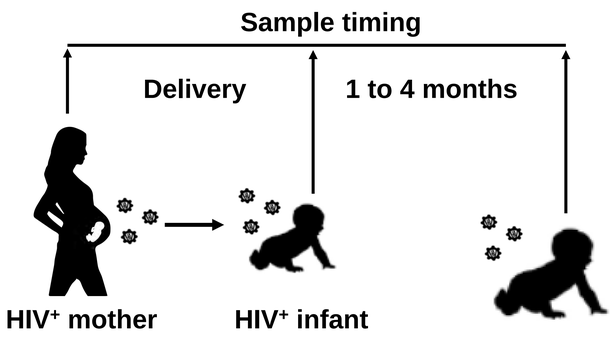
Manukumar Honnayakanahalli Marichannegowda[1], Michael Mengual[1], Amit Kumar[2], Elena E. Giorgi[3], David R. Martinez[2], Joshua J. Tu[2], Xiaojun Li[1], Sallie Permar[2], Feng Gao[1]

[1]Department of Medicine and [2]Duke Human Vaccine Institute, Duke University Medical Center Durham, NC, USA; [3]Los Alamos National Laboratory, Los Alamos, NM, USA

Background

- Mother-to-child transmission (MTCT) of HIV remains a global challenge; with 0.18 million infections in children during 2018.
- It is estimated that the one third MTCT occurs through in utero infection.
- The timing of in utero MTCT infection and selection pressure on viruses in infants during pregnancy are not well understood.

Methods



- Plasma samples were collected from 12 pairs of mothers (at delivery) and infants (at and post delivery) from the Women Infant Transmission Study (WITS) cohort and the CHAVI009 cohort.
- Viral RNA was extracted from mother and infant plasma samples.
- Complete HIV-1 *env* gene sequences were obtained by single genome amplification (SGA) from each sample and were used to study viral variation and evolution, infer transmitted/founder (T/F) virus sequences, estimate infection time, and identify selection sites in the *env* gene.

Results

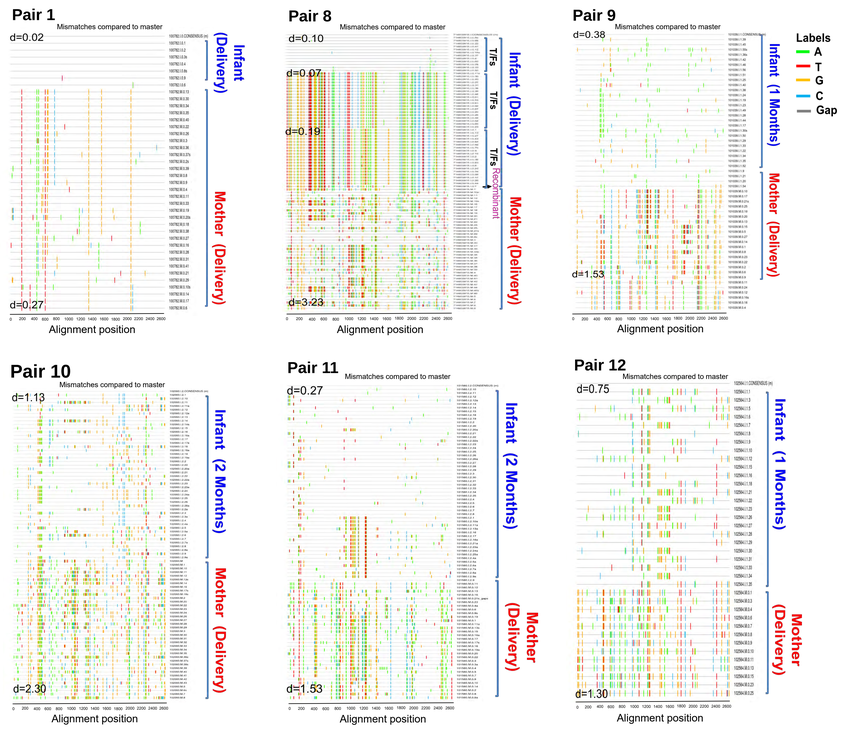


Figure 1. Highlighter plot analysis of the *env* sequences from 6 mother-infant pairs

Table 1. Demographic and genetic characteristics of mother-infant transmission pairs

Transmission Pair	Subject	Viral load (copies/ml)		No. of SGAs		No. of T/Fs	Infant age (days)	Estimated transmission time in days (95%, CI)	Transmission days from birth
		Mother	Infant	Mother	Infant				
1	100782	8,224	2,716	32	7	1	6	9 (4,15)	-3
2	101730	45,924	716,003	28	29	1	27	44 (33,54)	-17
3	100489	30,067	779,602	35	26	1	20	32 (21,44)	-12
4	101348	4,458	332,727	19	46	1	40	61 (52,70)	-21
5	714909112	NA	NA	34	21	1	1	20 (14,26)	-19
6	101744	276,955	NA	21	35	2	21	49 (29,69)	-28
7	100842	6,057	216,000	NA	37	2	20	27 (23,32)	-7
8	714903915	NA	NA	41	51	3	1	38 (35,41)	-37
9	101039	25,049	1,957,418	24	30	Chronic	39	NA	
10	102093	3,101,258	1,119,972	38	45	Chronic	54	NA	
11	101580	78,174	NA	32	53	Chronic	51	NA	
12	102564	26,640	NA	13	24	Chronic	28	NA	

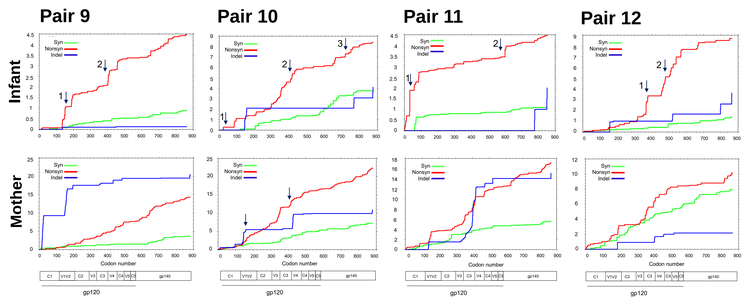


Figure 2. Accumulation of synonymous and non-synonymous mutations in viral populations from paired mothers and infants

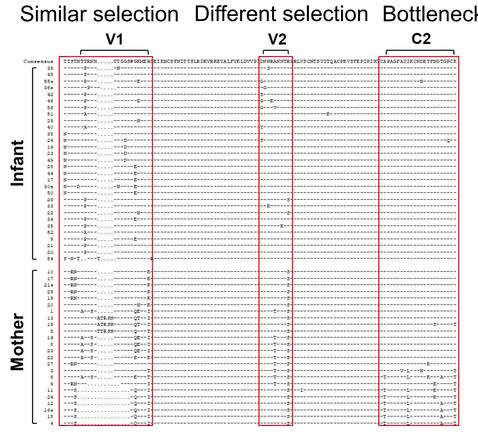


Figure 3. Selection sites and transmission bottleneck among infant sequences in pair 9

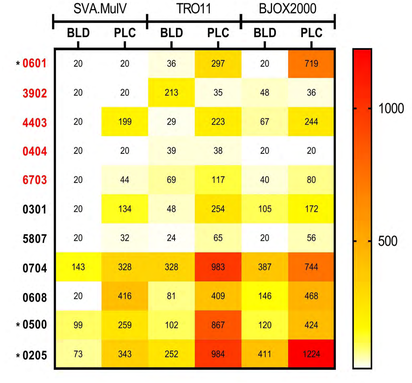


Figure 4. Stronger neutralization activity of placental blood plasma than the systemic plasma from the paired mothers

Conclusion

- The majority (8/12) of *in uterus* transmissions occur in the late third trimester during pregnancy (within two months from delivery).
- Selection signatures that are different from those in mother viruses can be detected in infant viruses, suggesting immune selection on infant viruses during pregnancy.
- Higher levels of neutralization activities in placental blood plasma may play an important role in driving virus evolution during pregnancy.