Human immunodeficiency virus type 1 (HIV-1) transmission through oral and gastrointestinal tissues is a well-documented route of infection in breastfeeding infants. The genetic and biological properties of viruses transmitted through breast milk have not been defined in an oral mucosal model. Objectives: To identify the genetic and biological phenotypes of viral variants transmitted through breast milk, we characterized the viral variants found in a mother-infant transmission pair. An ex-vivo model was used to evaluate whether tonsil tissue can support viral replication of breast milk derived virus. Methods: Virus stocks were prepared from the breast milk cells of a nursing HIV-infected Zimbabwe mother and the peripheral blood mononuclear cells of her 6-month-old infected infant. Using V1/V2- and V3-specific heteroduplex tracking assays (HTAs), we identified 3 major viral variants from the mother and 4 major variants from the infant. DNA fragments containing the V1-V3 gp120 region of each variant were generated by RT-PCR, rescreened in HTAs, analyzed by sequencing, and used to generate full-length infectious recombinant viruses within a NL4-3 backbone which were subsequently analyzed by a coreceptor usage assay. Recombinant viruses generated from breast milk were then tested in the human tonsil model and infection was monitored by cell associated p24 ELISA. Results: Recombinant viruses from both mother and infant contained unique yet highly related amino acid sequence patterns in the V1-V3 regions. Phylogenetic analysis revealed that one maternal variant was likely transmitted and subsequently evolved in the infant. The majority of recombinant viruses utilized the CCR5 coreceptor. All breast milk derived viruses were infectious in tonsil tissue. Conclusions: These findings suggest that a single CCR5-using maternal variant was transmitted to the infant. Genetic diversity was limited in viruses derived from the transmission pair. Tonsil organ cultures are a promising model to study breastfeeding HIV-1 transmission.

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