Cloning and characterization of functional subtype A HIV-1 envelope variants transmitted through breastfeeding.

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Abstract

Previous studies of HIV-1 variants transmitted from mother-to-infant have focused primarily on computational analyses of partial envelope gene sequences, rather than analyses of functional envelope variants. There are very few examples of well-characterized functional envelope clones from mother-infant pairs, especially from envelope variants representing the most prevalent subtypes worldwide. To address this, we amplified the envelope variants present in 4 mother-infant transmission pairs, all of whom were infected with subtype A and three of whom presumably transmitted HIV-1 during the breastfeeding period. Functional envelope clones were constructed, either encoding full-length envelope sequences from the mother and baby or by making chimeric envelope clones in a common backbone sequence. The infant envelope sequences were genetically homogeneous compared to the maternal viruses, and pseudoviruses bearing these envelopes all used CCR5 as a coreceptor. The infant viruses were generally resistant to neutralization by maternal antibodies present near the time of transmission. There were no notable differences in sensitivity of the mother and infant envelope variants to neutralization by heterologous plasma or monoclonal antibodies 2G12 and b12, or to inhibition by sCD4, PSC-RANTES or TAK779. This collection of viral envelopes, which can be used for making pseudotyped viruses, may be useful for examining the efficacy of interventions to block mother-infant transmission, including sera from vaccine candidates, purified antibodies under consideration for passive immunization and viral entry inhibitors.