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/SEQUENCE / VERTICAL TRANSMISSION

SUPORN FOONGLADDA : GENETIC AND BIOLOGICAL CHARACTERIZATION OF HIV-1 SUBTYPE E IN VERTICAL TRANSMISSION THESIS
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Vertical transmission of human immunodeficiency virus (HIV) is one of the major paths of AIDS epidemic spread. It is well known that the rate of HIV-1 vertical transmission varies from 14 to 39% in various geographic regions and 24.2% in Thailand.

To determine heterogeneity of envelope gene, heteroduplex mobility assay (HMA) of envelope gene (V1-V5) of HIV isoaltes from 30 transmitting mothers and 20 non-transmitting mothers was performed. Ninety percent of transmitting mothers (27/30) show high heterogeneity with heteroduplex mobility <0.9.

The variable region 3 (V3) of HIV-1 isolates from 30 transmitting mothers, 20 non-transmitting mothers and 31 infants were analyzed. Three to eleven clones were analyzed per subject. There was no significant difference between those of transmitting mothers and non-transmitting mothers. The genetic diversity of V3 region among mothers in each group was also similar. The V3 nucleotide distances of infaants comparing with their mothers more than 6% were significantly associated with immunosuppression of the infants in the first year of life.

From the observation of 35 amino acid sequences of V3 region, GPGQ at the tip of V3 loop was predominant and showed highly conserved sequences frome mothers to their infants. Asparagien (N)- linked glycosylation sites at positions 6 and 7 of the V3 loop were completely conserved in infants. N substitution at position 13 or/and 29 of the V3 loop were highly conserved in vertical transmission and significantly associated with the non-immunosuppression infants within the first year of life. All viral variants in this research were predicted to be non-SI phenotype.

Plasma HIV-1 RNA levels of all seven non-transmitting mothers were less than 4×10^4 copies/ml whereas those of 7 of 9 transmitting mothers contained more than 4×10^4 copies/ml. The other two transmitting mothers, who had plasma viral load lower than 4×10^4 copies/ml, had high genetic diversity of HIV-1 determined by HMA.

Viruses were isolated from of the transmitting mothers and two of the non-tansmitting mothers. Syncytium formation was observed by transmission electron microscope. Cells fusion appeared to be monocyte-lymphocyte or monocyte-monocyte.

No single parameter can adequately predict vertical transmission of HIV-1 subtype E.