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Poster presentation

Maternal neutralizing antibodies against a CRF01_AE primary isolate are associated with a low rate of intrapartum HIV-1 transmission in Thailand

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Background

Mother-to-child transmission (MTCT) of HIV-1 provides a model for studying the role of passively acquired antibodies in preventing infection. We previously hypothesized that broadly neutralizing heterologous antibodies (NAbs) would protect babies against intrapartum (IP) transmission. We measured NAb titers against primary isolates of various clades in sera from pregnant Thai women, and identified an association between higher titers of Nabs against a CRF01_AE primary isolate, MBA, and lower rates of IP transmission. Here, we extended our previous study using three CRF01_AE strains in a different Thai population, to confirm the association previously observed. We also investigated the molecular characteristics of the MBA envelope glycoprotein (Env) that might explain this association.

Methods

We measured and compared the titers of NAbs against six primary isolates (3 CRF01_AE and 3 clade B strains) in sera from 45 transmitting (T) and 45 nontransmitting (NT) Thai mothers matched for baseline viral load and duration of zidovudine prophylaxis, the two main independent factors associated with MTCT. We cloned and sequenced the *env* gene of the three CRF01_AE strains and compared the neutralization profiles by mothers' sera of pseudotyped viruses expressing wild type or chimeric Env proteins.

Results

Among CRF01_AE strains, MBA was more resistant to neutralization than the two other strains, LEA and C1712. The three clade B strains displayed similar neutralization profiles. We did not find an association between NAbs and MTCT for the three B strains or for LEA and C1712. In contrast, higher levels of NAbs against MBA were significantly associated with lower rates of IP transmission. The Env of this strain showed an unusually long V2 domain of 63 amino acids including six potential N-linked glycosylation sites. Using pseudotyped viruses expressing either MBA or LEA wild-type Env or a chimeric Env containing the V2 domain of MBA in an LEA Env backbone, we showed that the extended V2 domain contributed to the higher level of resistance to neutralization by mothers' sera in this strain.

Conclusion

This study confirms that higher titers of maternal NAbs against a CRF01_AE primary isolate, MBA, are associated with a lower IP risk of HIV-1 transmission in Thailand, and that the V2 domain of gp120 seems to have a major role in the neutralization process. We suggest that some

primary isolates may be useful indicators for identifying protective antibodies.