Poster presentation

Evolution of HIV-1 envelope sequences and coreceptor tropism during pregnancy

Doris Ransy[1,2], Josiane Couto[1,2], Bertine Akouamba[1,2], Johanne Samson[1], Normand Lapointe[1,3], Marc Boucher[1,4] and Hugo Soudeyns*[1,2]

Address: [1]CHU Sainte-Justine, Montreal, Quebec, Canada, [2]Department of Microbiology and Immunology, Université de Montréal, Montreal, Quebec, Canada, [3]Department of Pediatrics, Université de Montréal, Montreal, Quebec, Canada and [4]Department of Gynaecology and Obstetrics, Université de Montréal, Montreal, Quebec, Canada

* Corresponding author

Background
HIV-1 Env mediates viral entry into target cells and defines R5 or X4 phenotype. HIV tropism is important in pathogenesis and is associated with mother-to-child transmission. Env is under strong selective pressure within the host. The aim of this study was to determine whether changes in maternal immunity associated with initiation and progression of pregnancy influence Env sequence variation and HIV-1 coreceptor usage.

Methods
A longitudinal study of Env sequence variation was performed in 25 pregnant women infected with HIV-1 of clade B (n = 16) or non-B (n = 9). Viral RNA was extracted from plasma, the env gene (nucleotide positions 6430–7374) was PCR-amplified and subcloned, and a mean of 20 clones were sequenced per trimester of pregnancy. HIV tropism was predicted in silico using $PSSM_{X4R5}$, $PSSM_{SINSI}$, SVM, geno2pheno and charge rule algorithms. Phylogenetic reconstructions were built, sequence diversity was estimated using p distances and selective pressure (dN/dS) was computed.

Results
In study subjects, HIV-1 viral load decreased progressively during the course of pregnancy. Envelope sequences were amplified at all trimesters in 63% of the cases. Phylogenetic analysis revealed at least partial clustering of sequences per trimester in 4 out of 9 patients. Nucleic acid p distances were negatively correlated with CD4+ T cell counts at study entry (r^2 = 0.66, p = 0.02). In all clade B variants examined, R5 phenotype was predicted by all algorithms. Interestingly, while predictions were not as consistent with non-B subtypes, R5 and X4 variants were shown to coexist during pregnancy in 4 of 5 cases. Of note, evolution of tropism from R5 to X4 was observed in one subject, and evolution from dual tropism to exclusive X4 was observed in another subject between two consecutive pregnancies. Higher levels of genetic diversity in the V2 region were observed in subjects infected with non-B subtypes as compared with clade B variants. Finally, selective pressure on V2 tended to decrease with time in subjects infected with the B subtype but remained relatively high in sequences derived from carriers of non-B subtypes.

Conclusion
This study provides insights into the possible interplay between viral population dynamics and selective pressures exerted by maternal HIV-1 specific immune response during pregnancy, insights that could prove invaluable for the development of active and/or passive immunization strategies to prevent mother-to-child transmission of HIV-1.