Retrovirology

BioMed Central

Oral presentation

Influence of pregnancy on the specificity and breadth of antigen recognition by HIV-specific cytotoxic T lymphocytes

Elyse Jolette*[1,2], Johanne Samson[3], Normand Lapointe[3,4], Marc Boucher[3,5] and Hugo Soudeyns[1,2,4]

Address: [1]Unité d'immunopathologie virale, CHU Sainte-Justine, Montreal, Quebec, Canada, H3T 1C5, [2]Department of Microbiology & Immunology, Université de Montréal, Montreal, Quebec, Canada, H3C 3J7, [3]Centre maternel et infantile sur le SIDA, CHU Sainte-Justine, Montreal, Quebec, Canada, H3T 1C5, [4]Department of Pediatrics, Université de Montréal, Montreal, Quebec, Canada, H3C 3J7 and [5]Department of Gynecology & Obstetrics, Université de Montréal, Montreal, Quebec, Canada, H3C 3J7

* Corresponding author

from Fourth Dominique Dormont International Conference. Host-Pathogen Interactions in Chronic Infections
Paris, France. 13-15 December 2007

Published: 9 April 2008

Retrovirology 2008, **5**(Suppl 1):O7 doi:10.1186/1742-4690-5-S1-O7

This abstract is available from: http://www.retrovirology.com/content/5/S1/O7

Background

Mother-to-child transmission (MTCT) of HIV-1 is one of the major issues of the pandemic. Characterization of HIV-specific immunity during pregnancy, especially cytotoxic T lymphocytes (CTL), will lead to a better understanding of HIV pathogenesis and facilitate design of optimal strategies to prevent MTCT. Our objective is to define the influence of initiation and progression of pregnancy on the antigenic specificity and breadth of antigenic recognition by HIV-specific CTL.

Materials and methods

Study subjects were women infected with B or non-B HIV-1 subtypes who underwent successive pregnancies (n=11) or wanted to become pregnant (n=4). Median age at study entry was 27.8 years and median CD4 count was 490 cells/mm^3. All subjects were treated with combinations of antiretroviral agents for maternal health and to prevent MTCT. Antigenic specificity of CTL was evaluated on serially-obtained (1st, 2nd, 3d trimesters) CD4-depleted samples of peripheral blood mononuclear cells using IFN-γ enzyme-linked immunospot assay (ELISpot). Screening was performed with synthetic peptide matrices (20 amino acids with 10 residue overlap) corresponding to Gag sequences from HIV-1 clades A, B, C and D. Breadth of antigenic recognition was defined as the number of peptide pools showing positive CTL reactivity.

Results

Significant variations were observed in the magnitude of HIV-1 Gag-specific CTL responses, which ranged between 15 and 1,350 spot-forming units (SFU)/100,000 cells. Variations in the breadth of antigenic recognition were also observed, with 2-11 peptide pools generating CTL reactivity. These differences were evidenced before and after initiation of pregnancy, as well as between trimesters of gestation, and were seen in all patients irrespective of the clade of the infecting HIV-1 variant (B, D, or CRF02_AG), the number of antiretroviral agents used (n=2-6), and the control of HIV-1 viral load. In all cases, CTL were targeted to Gag regions that contained known CTL epitopes.

Conclusions

These results indicate that pregnant HIV-infected women generate robust HIV-specific CTL responses that are capable of simultaneously targeting multiple antigenic determinants, inconsistent with a broad dysfunction of cell-mediated immunity in pregnancy. These CTL responses exhibited longitudinal variations in terms of antigenic specificity and breadth of antigenic recognition, variations that could be explained by sequential waves of expansion and contraction of CTL clones of mixed antigenic specificity and/or continuing viral escape from CTL responses. These results provide a novel understanding of the dynamics of HIV-specific CTL responses during pregnancy and may help to promote maternal immunization as a strategy to prevent MTCT of HIV-1.