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degree of cross-reactivity of the HIV-specific immune responses between different HIV clades.
Objective : To determine if HIV-1 specific CTL from patients infected with different HIV-1 clades can recognize and lyse target cells infected with viral constructs expressing clade A-, B, or C gene products.
Methods : Frozen PBMC from North-American and African patients infected with HIV-1 were antigen specifically stimulated. Effectors were tested against autologous B-LCL targets infected with vaccinia recombinant virus expressing HIV-1 env, gag and pol genes from different clades using a conventional 4-hour chromium release assay. Levels of CTL responses were measured in bulk assay or by limiting dilution analysis (LDA).
Results : Memory CTL from HIV-1 infected North-American or African patients recognized target cells expressing HIV-1 env, gag and pol genes from clades A, B, and C. Levels of CTL responses vary between patients and the gene expressed by target cells. Maximum responses were observed against targets expressing gene specific for the HIV-1 clade of the infected individual.
Conclusion : Our study demonstrates that HIV-1 specific CTL epitopes are conserved between clades and suggest that a vaccine based on a single clade may induce cross-reactive cellular immune responses with other clades.

A. 316 Cytotoxic T Lymphocytes (CTL) From HIV-2 positive Patients Frequently Cross-React With Different HIV-1 Subtypes

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Knowledge of the immune mechanism responsible for the cross-protection between divergent viruses such as HIV-1 and HIV-2 may help to understand whether virus variability may be overcome in the design of vaccine candidates which are protective across the HIV subtypes. We used polyclonal CTL lines from 18 HIV-2 infected subjects to define whether a dominant CTL response has the ability to recognize the HIV-1 virus. CTLs were initially tested against products of HIV-2 gag, pol and nef genes. A clear immunodominance (15/18 patients) of CTL response against gag protein was present. We then analysed the ability of selected gag specific-CTL lines from 11 patients to recognize different HIV-1 gag subtypes and we found that, despite the significant difference in virus amino acid sequence between the heterologus viruses, the majority (9/11) of HIV-2 subjects do have CTL able to lyse the target cells expressing HIV-1 gag protein. This work suggest that the immunity against HIV-2 may enhance the immune system's ability to react to HIV-1 which may play a role in cross-protection.

A. 317 Identification and Characterization of Potent HIV-1 Sera Able to Neutralize 17 Primary HIV-1 Isolates Belonging to group M (Subtypes A-H) and Group O

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Objective : The main aim of this study was to identify patients with poten cross-neutralizing sera against 17 primary isolates belonging to HIV-1 group M (subtypes A-H) and group O.
Materials and Methods : A total of 67 sera (66 HIV-1 sera, 1 HIV-1+2 serum, 51 men, 14 women, and 2 unknown gender) were examined for their potency to neutralize three key isolates (MN, VI525, CA9) in fresh PHA-stimulated PBMCs. The potency of a serum is defined as the logarithm of the geometric mean of the neutralizing antibody titers for each of the primary isolates tested. Sera which were able to neutralize all three key isolates, were further examined for their cross-neutralizing Capacity using 14 other isolates belonging to group M (subtypes A.H) and group O. Fifty and ninety percent inhibitory does (ID50 and ID90) were defined as the highest serum dilution that produced > 50 and > 90% reductions in p24 antigen production.
Results : Out of 67 patients (51 men, 14 women, and 2 unknown gender), 8 sera with the capacity to neutralize the three key isolates were identified. Seven of the eight sera were of female patients. These sera were able to neutrlize all 14 other primary isolates with high potency. IgG mediate the neutralizing activity since it could be absorbed to and eluted from protein G columns.
Conclusion : We were able to identify 8 HIV-1 patients with potent neutralization capacity against 17 HIV-1 isolates representing group M (subtype A-H) as well as group O. Seven out of eight were female. We could identify the neutralizing capacity as being antibody related. The data confirmed our previous findings that only 3 key HIV-1 isolates allow discrimination of sera that are likely or unlikely to neutralize primary isolates from most of the genetic clades (p Nyambi et al. Virol 1996, 70, 6235-6243).

A. 318 HIV Specific Mucosal and Seric IgA in Pregnant Women in North Uganda

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Heterosexual transmission is one of the most frequent route of HIV transmission in Africa. HIV specific mucosal immunity, both humoral and cellular-mediated has been demonstrated in animal studies ; recently, by our group, env-HIV specific mucosal IgA were demonstrated in 82% of seronegative heterosexual individuals repeatedly exposed to HIV infection (Nat. Med. Submitted and accepted) in a minority of Health controls. IgA were the test of choice in detecting HIV exposure and protection to HIV in seronegative individuals, while it represented a confirmatory test in HIV seropositives. In this study we focused at the mucosal and seric IgA immune responses in a group of 22 pregnant women (P.W.) attending the Antenantal Clinic of St. Mary's Lacor Hospital in the Gulu district, Uganda. The contact and ingestion of maternal blood and cervico vaginal HIV infected secretion at delivery represent the most frequent feto-maternal route of HIV transmission. Thus maternal IgA may play a crucial role in

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protection of newborns during and after delivery during breast feeding, so important in Africa culture as nutritional factor. HIV specific IgA were detected in sera and in cervico-vaginal secretions of all the pregnant women by Western Blot (WB) (Sanofi Pasteur, France ; Cambridge, USA) and an ELISA env-HIV specific method (Calypte Biomed., USA- 3 out of the 22 P.W. (13.6%) resulted HIV seropositive and 19 seronegative in WB according to the WHO criteria . 54.5% (12/22) of the P.W. were env-HIV specific IgA positive in vaginal secretions by ELISA test and were WB confirmed, showing several immunisation env and core proteins bands, with a highly significant difference $p< 0.001$ (OR 9.6, CI : 2.7-33.6) if compared to a population of 45 Italian P.W. ; 6 out of the 22 were HIV-specific IgA positive in sera and 4 of them belonged to the HIV seronegatives. Cumulative positivity for IgA in secretion and sera was 72,7% (16/22). Among the HIV seropositives 13/19, 68, 4% tested HIV-specific IgA positive demonstrating a high exposure rate to HIV by heterosexual contacts. IgA positivity in vaginal secretion was not associated with serum IgA positivity, postulating a compartimentalised immune response at HIV infection site. Sexual exposure was supported by a high HIV specific IgA positivity rate, 88.9% in women with other STDs if compared with STDs negatives (OR 5.7 ; CI 0.5-61.4). The presence of an high positivity rate for HIV specific IgA, especially at mucosal site in this seronegative P.W. population demonstrates an high risk of exposure to the virus in African healthy populations and open new perspectives for a possible protective role of this secretory antibodies, especially during pregnancy and for future mucosal strategy of vaccination in African populations