

Cryptic C2V3C3 epitopes in the HIV-1 envelope prevent cross-reactivity with antisera from HIV-2 infected patients

B. Costa^{1,2,3}, I. Bártoło³, H. Barroso^{2,3}, N. Taveira^{2,3}, A. I. Fernandes^{1,2}

¹Centro de Polímeros Biomédicos; ²Instituto Superior de Ciências da Saúde Egas Moniz, Monte de Caparica, Portugal; ³Centro de Patogénese Molecular, FFUL, Lisboa, Portugal

Human Immunodeficiency Viruses types 1 and 2 are known to have similar biological properties. Moreover, there are some conserved structures between HIV-1 and HIV-2 that can serve as target epitopes for the humoral immune response. Most of the neutralizing antibodies produced in HIV-1 and HIV-2 infected individuals are directed against epitopes located within the C2V3C3 domain (C2C3). Thus, cross-reactivity of HIV-1 and HIV-2 human antisera with HIV-1 and HIV-2 C2C3 polypeptides would be expected. In order to explore this possibility, the *env* gene region coding for the C2C3 domain was amplified by PCR from proviral DNA of three HIV-1 and three HIV-2 infected patients. Patients infected with HIV-1 subtype B, C and G or HIV-2 group A were selected for amplification. Amplification products were cloned into the expression plasmid pTrcHis A and several expression systems were obtained after competent *E. coli* transformation. Six new recombinant polypeptides representing the C2C3 region of the envelope glycoprotein of both HIV-1 and HIV-2 were obtained after expression by IPTG induction followed by a purification step by immobilized metal affinity chromatography. With respect to amino acid sequence, the HIV-1 and HIV-2 recombinant polypeptides showed no more than 50% of inter type homology. Two different serological methods - western blotting and enzyme-linked immunosorbent assay - were performed to evaluate the presence of linear antigenic epitopes on this region of both viruses. Our data shows that all C2C3 recombinant polypeptides cross-react with the correspondent HIV antisera from HIV infected patients. The recombinant polypeptides from HIV-1 subtypes B, C and G cross-reacted with HIV-2 antisera. However, similar cross-reactivity was not observed with HIV-2 polypeptides and HIV-1 antisera. These results suggest that some antigenic epitopes in the C2C3 region of HIV-1 are poorly immunogenic, probably because they are hidden from the immune system during infection. On the other hand, the equivalent target epitopes are exposed in the HIV-2 virus particle and may determine the nature of the humoral immune response to this virus (neutralizing and/or binding antibodies). In conclusion, our results suggest that either HIV-1 or HIV-2 C2C3 polypeptides should be further explored as vaccine immunogens.

This work was supported by a research grant from FCT and FEDER (POCTI/FCB/47407/2002).

Bruno Costa, Phone number: +351934900017, Meeting Code: X6, Poster Session: 1