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Evaluation of neutralizing anti-HIV-1 response in individuals infected by viral subtypes prevalent in Brazil in relation to genetic and biochemical characteristics of the env gene

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It is expected that an HIV vaccine/aids be able to induce specific response in CD8+ T cells and neutralizing antibodies (nAb). However the high genetic variability of the virus envelope gene (env) is one of the factors that can influence the ability of a vaccine. Thus, in order to assess humoral immune response against immunogens, HIV-1 neutralizing antibody detection assays have been used. Therefore, this study aims to evaluate the humoral immune response in individuals with different AIDS progression profiles and map the env gene characteristics of HIV-1 subtypes prevalent in Brazil. To this end, we performed a comparison between two neutralization assays, one using the viral isolate HIV-1IIIB in primary lymphocytes and the other neutralization with TZM-bl cells tested against eight pseudovírus (psVs). In these assays were tested 10 plasma samples obtained from individuals with typical profile of progression to aids and 10 from long-term non progressors (LTNP). In the first analysis, we observed 44% of neutralizing antibody titers against psVs and 50% for HIV-1 IIIB. The plasma samples from progressors showed broad and potent neutralization. From these results, we noted the importance of continuous antigenic stimulus in inducing humoral response and their influence for viral factors. Thus, we evaluated the genetic and phenotypic characteristics HIV-1 env subtype-specific and associated them to the induction of neutralizing activity. For this purpose, we selected 60 plasma samples from individuals infected with HIV-1 subtypes prevalent in Brazil and perform neutralization assay with psVs (same HIV-1 subtype). We observed a greater breadth and potency of anti-Env neutralizing response in individuals infected with the F1 or B HIV-1 subtypes compared with the C subtype and variant B/Bbr. We observed that the regions V1 from B/Bbr subtype had greater number of amino acids than the other subtypes and V4 region from F1 subtype had fewer amino acids ($p < 0.005$). We also observed that some subtype-specific signatures of F1 subtype and B/Bbr samples located in regions C2, V3 and gp41 may have influenced in the neutralizing response difference between them. These results indicate that a single amino acid substitution in the V3 loop may lead to a distinct conformational exposure or load, in association domain of trimer of gp120, and interfere with the neutralizing response potency and has a significant implication for the vaccine design.

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