Abstract

HIV-1 subtype C envelope-based peptide constructs as potential vaccine component

by

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The development of an effective HIV vaccine is hindered by several obstacles. One of the leading challenges is the antigenic variability of HIV-1 that is exhibited throughout all viral gene products but to greatest extent in the viral envelope proteins. This phenomenon is the result of continuous mutations in the HIV genome and is responsible for the immune escape of viral mutants. Many studies have suggested that a multivalent vaccine that elicits broadly cross-reactive antibodies is required to efficiently target antigenic variability. To this end, we have designed and analyzed a synthetic peptide construct that mimicked the major variability exhibited in the V3 loops of HIV-1 subtype C isolates. The peptide construct, described as a multiple epitope immunogen of the V3 loop with 8 branches and termed MEIV3b$_8$, was shown to be non-toxic but highly immunogenic in experimental animals (mice and rabbits) and produced antibodies that were reactive to V3 loop peptides of various subtypes, variant envelope proteins and whole viral isolates [at antibody titers $\leq$ 1000 in enzyme-linked immunosorbent assays (ELISAs)]. Furthermore, functional antibodies were generated in rabbits that mediated neutralization of a neutralization-sensitive HIV-1 isolate and two distinct primary HIV-1 isolates in several different neutralization assays (at antibody titres $\leq$ 1213). Additionally, the MEIV3b$_8$ induced both proliferative and inflammatory immune responses in a murine model.

Finally, antibodies in the plasma of individuals (n = 148) infected with HIV-1 subtype C, subtype B and HIV-2 were found to bind to the MEIV3b$_8$ as antigen in ELISAs. Through these findings, this study demonstrated that the variable MEIV3b$_8$ effectively addressed antigenic variability and provided evidence that this peptide construct may hold application in HIV-1 preventative and therapeutic vaccination as well as HIV immunodiagnosis.