Targeting conserved broadly neutralizing epitopes within HIV-1 envelope gp41 MPER as vaccine immunogens for seronegative partners of HIV-1 discordant couples

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Introduction: The membrane proximal external region (MPER) of HIV-1 envelope glycoprotein-41 (gp41) is targeted by several broadly neutralizing antibodies whose conserved linear epitopes are promising targets for vaccine design. However, a formidable challenge has remained the difficulty to design and deliver MPER based immunogens for the efficient induction of such broadly neutralizing HIV-1 specific antibodies (bnAb). This is mainly because the linear bnAb MPER epitopes are poorly accessible to the immune system. The overall objective of this study therefore was the development and validation of an RNA coliphage Qβ display system for efficient presentation of conserved bnAb epitopes to the immune system

Method: To overcome the challenge of effective presentation of MPER to the immune system we have selectively engineered the surface of the RNA coliphage Qβ to to display 12 molecules of MPER per phage particle. The expression cassettes were used for the production of QβMPER recombinant hybrid phages after transformation of E. coli HB101 strain.

Results: Specific recognition of all the linear MPER based bnAb epitopes were confirmed in ELISA with QβMPER VLP as antigen and the bnAb 2F5, Z13, 4E10 and 10E8 as antibodies. Next the prevalence of MPER specific antibodies was determined in plasma from antiretroviral naïve HIV infected participants of the CIRCB AFRODEC cohort. The greater majority (84%) of participants' plasma showed MPER peptide specific reactivity with antibody titers ranging from 200 to 409600 comparative to background values with Qβ empty as antigen.

Conclusion: Thus, this novel QβMPER VLP can be used to monitor MPER- specific immune responses in clinical samples. In addition the QβMPER VLP can be used as immunogens either alone or in combination with other strategies for the induction of MPER specific immunity against HIV-1.

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