Editorial
Volume 12:7, 2021

Journal of AIDS & Clinical Research

ISSN: 2155-6113 Open Access

Editorial Note on Developing an HIV Vaccine: Vaccinology Research

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Editorial

It is widely acknowledged that eradicating HIV from the human population will necessitate the development of an effective vaccine. Candidate vaccines that have been tested to date, on the other hand, have either failed or demonstrated very low and debatable efficacy. New vaccine trials based on producing both antibodies and T cell immunity have begun, and the findings of these trials will be known in the coming years. Simultaneously, a large body of evidence suggests that broadly neutralising antibodies (bnAbs) are created in natural HIV infection and that such antibody, delivered via passive transfer, can protect against HIV in animal models as well as alter HIV infection in humans.

The CD4-binding site (CD4bs) and the gp120–gp41 interface region are two bnAb-binding sites found on the HIV Env spike protein (which is made up of three gp120s and three gp41s in a trimer of non-covalently connected heterodimers). VRC34 is a bnAb that binds an epitope consisting of the eight amino-terminal residues of the fusion peptide (FP; residues 512–527 of gp41 that causes membrane fusion). They developed enhanced immunogens and vaccination techniques, now employing both FP and an SOSIP trimer, to elicit second-generation antibodies that neutralise up to 31% of HIV strains in mice, based on sequence analyses and structural research. The new regimens were then put to the test in nonhuman primates (NHPs).

Three of five sera from vaccinated NHPs demonstrated neutralisation breadth at a dilution of 1:20, with one serum neutralising roughly 22% of HIV strains well. This is far from ideal, but given the relative simplicity of the immunogens and immunisation regime, it's a promising start, and it's sparked a lot of new interest in FP as an HIV vaccine target. Given the combination of efficacy and breadth demonstrated by CD4bs-specific bnAbs, CD4bs is likely the most popular bnAb target. The VRC01 class of CD4bs-specific bnAbs utilises a single immunoglobulin heavy (H) chain variable (V) germline gene segment (VH1–2), making immunogen design for this class of bnAb extremely simple.

How to cite this article: Stewart, Eleni. "Editorial Note on Developing an HIV Vaccine: Vaccinology Research." J AIDS Clin Res 12 (2021): 850.

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Received 15 July 2021; **Accepted** 20 July 2021; **Published** 25 July 2021