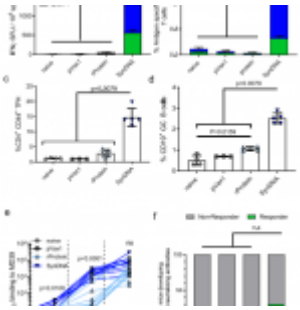
HIV vaccine progress



In a recent paper, Ziyang, et al., have produced novel insights into and further developed an HIV vaccine through the use of a unique trimer in order to develop Tier-2 neutralizing antibodies within a murine model.

HIV, a deadly virus that researchers today are still trying to understand, has killed 36.3 million people worldwide. A vaccine, key to preventing the spread and combatting severity of the virus, is still far from development. However, in this present study published in *Nature Communications,* researchers have made significant strides into the development of a promising vaccine therapy.

In the past it was extremely expensive and time-consuming to investigate the efficacy of these types of antibodies within animal models, but in this study they have established a faster method, developing a new model to produce Tier-2 neutralizing antibodies in mice. Engineering the trimer into DNA for transfection into mice, this method induces antigen production within the host without the need to manufacture a vaccine. Through comparison between mice who received the DNA-encoded native-like trimer with mice who received a standard protein immunisation, they reported that only the mice receiving the DNA-encoded native-like trimer developed Tier-2 neutralizing antibodies (Figure 1).

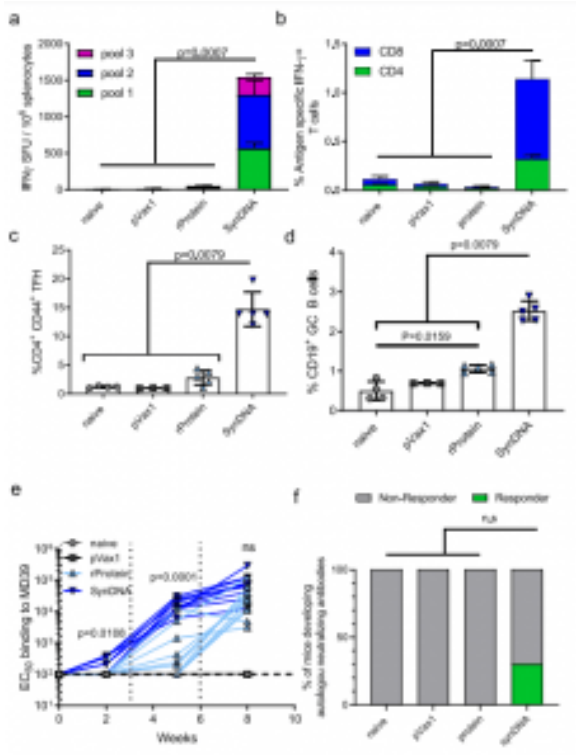


Figure 2: DNA immunization of BG505.MD39 induced stronger T-cell responses and NAb responses than protein immunization in BALB/c mice. *All mice in this panel were immunized at Wks 0, 3, 6 with 25 ug DNA or 25 ug RIBI-co-formulated protein and euthanized 2 weeks post the final vaccination for cellular analyses. a, b Comparison of BG505 Env-specific cellular responses in naïve mice, or mice immunized with pVAX plasmid backbone, RIBI-coformulated protein BG505.MD39, or DNA-encoded BG505.MD39 by IFNγ ELIspot assay (a) or intracellular cytokine staining (b). c*

Frequencies of CXCR5 + PD1 + Tfh cells amongst CD4 + CD44 + cells in the draining lymph nodes in naïve mice or 10 days post pVAX1, protein MD39 or DNA BG505.MD39 immunization. d Frequencies of GL7 + GC B cells amongst CD19 + B cells in the draining lymph nodes in naïve mice or 10 days post pVAX1, protein BG505.MD39 or DNA BG505.MD39 immunization. e Trimer-specific binding antibody responses induced in mice vaccinated with protein or DNAencoded BG505.MD39 post the first, second and third immunization as determined by ELISA. f Frequencies of mice that developed autologous BG505.T332N neutralizing antibodies (ID50 titers greater than 1:45) in naïve mice or mice immunized with pVAX1, protein BG505.MD39 or DNA-encoded BG505.MD39 two weeks post the final vaccination. The dashed vertical line in e refers to the immunization timepoints. Two independent experiments were performed for each panel in the figure. N = 10 mice/group for protein or DNA-encoded

BG505.MD39, N = 5 mice/group for naïve mice or pVAX1 treated mice (a, b, e, f); N = 5 mice/group (c, d); each dot or line represents an animal. Error bar represents standard deviation. Center of the error bar represents the mean. Two-tailed Mann–Whitney Rank test used to compare groups; p-values were adjusted for multiple comparison for panels (a–d). Twotailed Mann–Whitney Rank tests were used to compute the p-values comparing EC50 titers between protein and DNA groups for each specific timepoint in e. Two-sided Fisher Exact Tests were used to compare proportion of responders between SynDNA group and naïve/ pVAX1/ protein groups in f. ns not significant. Source data are provided as a Source Data file (Ziyang, et al., 2022).

Following confirmation of the production of Tier-2 antibodies, Ziyang, et al., proceed to investigate the atomic structure of one Tier-2 neutralizing monoclonal antibody using cryo-EM. They were able to describe how the antibody is able to neutralize the virus providing insight into how one may *design new vaccines that can generate broadly neutralising antibody responses to the C3V5 epitope.*

In such a promising study, engineering and delivering these

immunogens via nucleic acid technology into a vaccinated animal, is a massive step in the right direction. These *in vivo* self-assembly of structurally designed immunogens may allow us the ability to tailor certain vaccines.

Journal article: Ziyang, X, et al., 2022. Induction of tier-2 neutralizing antibodies in mice with a DNA-encoded HIV envelope native like trimer. *Nature Communications*.

Summary by Stefan Botha