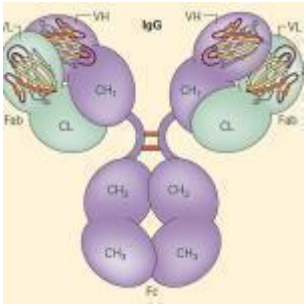
Do we need to re-think vaccine strategies to elicit anti-HIV antibodies?



A vaccine that can elicit neutralizing antibodies to HIV, and thus lead to protection from infection, is the holy grail of vaccinology. However, we know that HIV mutates rapidly to avoid detection by antibodies. Antibodies can also mutate at similar rates and this virus: antibody variation represents a "race" between host immunity and pathogen.

In the latest edition of PLoS Biology, Patricia Gearhart and colleagues, have written a short essay on the specialized proteins and error-prone polymerases that change antibody DNA sequences. They explore how B lymphocytes express activation-induced deaminase (AID), which causes a large wave of "mutations in the immunoglobulin loci", that results in random DNA substitutions. This is then followed by "selection for the highest affinity antibodies" in a process known as affinity maturation and in HIV infection, this can take several years to develop.

The authors propose a prophylactic vaccine strategy of using a "plethora" of engineered antigens to develop a large repertoire of long-lived primed memory B cells. This would elicit a "diverse set of variable genes with a few mutations…. and generate antibodies with low affinity for HIV.

A second layer of immunity can be elicited with a boost of a

lower dose of a specific antigen, which would serve to focus the antibody response to a mutated, or different subtype of virus. This approach serves to select for “rare cross-reactive B cells or heteroclitic B cells from the expanded repertoire”. The heteroclitic antibodies produced can then bind strongly to antigens with little or no similarity and could be a useful preventative vaccination approach to elicit broadly neutralizing antibodies to HIV. Although an attractive approach, the fear of inducing auto-reactive antibodies would need to be closely monitored.

Gearhart, P. et al. 2015. Exceptional Antibodies Produced by Successive Immunizations. *PLOS*.