

AIDS VACCINES AT A CROSSROADS: WHAT MIGHT THE FUTURE HOLD?

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The continued HIV-1 pandemic underscores the need for an effective AIDS vaccine. Advances in our basic understanding of the immune system have provided the tools to develop rationally designed vaccines based on a scientific understanding of the mechanisms of microbial pathogenesis and immunity. Current HIV vaccine candidates target multiple internal and external gene products. Next generation vaccines will need to enhance immunogenicity of the envelope (Env), with the goal of improving the breadth of the neutralizing antibody response while concurrently stimulating cell-mediated immunity, which can potentially control virus replication at the portal of entry or inhibit replication of viral variants that are less sensitive to neutralization. Recent efforts have centered on the use of genetic and structural biological information to improve both Env and Gag immunogen design. The genetic approach has focused on the conserved regions of Gag and Env to improve CD8 cell breadth. To target such conserved domains, site-specific mutagenesis has been employed to generate and analyze mosaic, variant, and chimeric Env and Gag proteins. Nonhuman primate models are useful in identifying potential T cell vaccines, while vaccine efficacy in human studies is undergoing preliminary exploration. This dual approach of eliciting cellular and humoral immunity in AIDS vaccines offers the greatest potential to control the spread of HIV-1.