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New Paradigms for HIV/AIDS Vaccine Development

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Abstract

HIV-1 and its simian counterpart SIV have been exquisitely tailored by evolution to evade host immunity. By virtue of specific adaptations that thwart individual innate or adaptive immune mechanisms, and an overall replication strategy that provides for rapid establishment of a large, systemic viral population, capable of dynamic adaptation to almost all immune selection pressures, these viruses, once established, almost invariably stay one step ahead of the host, and in the vast majority of infected individuals, replicate indefinitely. Although many of vaccine approaches tested to date have been able to enhance the magnitude of the immune responses to HIV/SIV infection, most of these responses, whether cellular or humoral in nature, have largely failed to be both effectively anti-viral and targeted such that fully functional escape variants are not easily selected. Recent advances, however, have provided strong evidence that the initial stages of infection following mucosal transmission of these viruses are more vulnerable to immune intervention, and have led to the development of vaccine strategies that elicit responses able to effectively intervene in these early stages of infection, either preventing acquisition of infection or by establishing early, stringent, and durable control. Here, we place HIV/AIDS vaccine development in the context of the basic immunobiology of HIV/SIV, review the evidence for the vulnerability of early infection to immunity, and discuss how these newly recognized immune vulnerabilities might be exploited for the development of an effective HIV/AIDS vaccine.

Keywords

HIV/SIV; T cell vaccines; antibody vaccines; immune evasion; nonhuman primate models; persistent vectors; immune clearance

Introduction

HIV-1 infections of humans and pathogenic SIV infections of nonhuman primates (NHP) share a pattern of viral replication and a constellation of pathological features that in the absence of anti-retroviral therapy almost always result in unceasing infection and a progressive, ultimately fatal, immune deficiency (1-3). A striking feature of these pathologic lentiviral infections is their induction of robust cellular and humoral immune responses,

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DISCLOSURE STATEMENT

The authors declare the following competing financial interests: OHSU has licensed CMV vector technology, for which LJP and SGH are inventors, to the International AIDS Vaccine Initiative (IAVI).

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Annual Review Of Medicine 63

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