HIV: Current Research

Extended Abstract

Merck Ad5/HIV induces broad innate immune activation that predicts CD8$^+$ T-cell responses but is attenuated by preexisting Ad5 immunity

Alan Aderem

Abstract

To better understand how innate immune responses to vaccination can lead to lasting protective immunity, we used a systems approach to define immune signatures in humans over 1 wk following MRKAd5/HIV vaccination that predicted subsequent HIV-specific T-cell responses. Within 24 h, striking increases in peripheral blood mononuclear cell gene expression associated with inflammation, IFN response, and myeloid cell trafficking occurred, and lymphocyte-specific transcripts decreased. These alterations were corroborated by marked serum inflammatory cytokine elevations and egress of circulating lymphocytes. Responses of vaccines with preexisting adenovirus serotype 5 (Ad5) neutralizing antibodies were strongly attenuated, suggesting that enhanced HIV acquisition in Ad5-seropositive subgroups in the Step Study may relate to the lack of appropriate innate activation rather than to increased systemic immune activation. Importantly, patterns of chemo attractant cytokine responses at 24 h and alterations in 209 peripheral blood mononuclear cell transcripts at 72 h were predictive of subsequent induction and magnitude of HIV-specific CD8$^+$ T-cell responses. This systems approach provides a framework to compare innate responses induced by vectors, as shown here by contrasting the more rapid, robust response to MRKAd5/HIV with that to yellow fever vaccine. When applied iteratively, the findings may permit selection of HIV vaccine candidates eliciting innate immune response profiles more likely to drive HIV protective immunity.

Keywords: immunology, innate immunity, systems biology, systems vaccinology, immunogenicity

Alan Aderem
Department of Immunology
Seattle Biomedical Research Institute, Seattle
E-mail: alan.aderem@seattlebiomed.org