Universal, MHC-E Restricted Killer T Cell Responses: Identification of a Novel Immune Response against HIV

Pathak, Reesab

With over 34 million people living with HIV today, a prophylactic vaccine is urgently needed.Due to a history of vaccine failure, a novel vaccine modality is necessary. Researchers studying HIV commonly use Simian Immunodeficiency Virus (SIV) in Rhesus macaques as a reliable model for HIV infection.Recently, a vaccine targeting SIV showed an unprecedented fifty percent efficacy in vaccinated macaques with protected animals completely clearing viral infection. This vaccine utilizes a recombinant strain of Rhesus cytomegalovirus (RhCMV), which induces unique immune responses.A subset of vaccine-induced, major histocompatibility complex (MHC)-class II-restricted CD8+ (killer) T cell responses breaks a central tenet of immunology. However, the engendered MHC-class I-restricted responses remained uncharacterized. The research here uses laboratory-designed antigen presenting cells expressing single MHC class I molecules in ex vivo CD8+ T cell restriction assays to show that the non-classical Rhesus MHC-E molecule restricts RhCMV/Gag vaccine-induced CD8+ T cell responses. Rhesus MHC-E is highly conserved with its human ortholog HLA-E and has low polymorphism, especially in comparison to classical MHC-I molecules. The limited sequence diversity in MHC-E explains the universal targeting seen in RhCMV-vaccinated macaques. This suggests that epitopes thought to be restricted by multiple MHC molecules, termed “supertopes,” might instead be presented by MHC-E. Notably, MHC-E-restricted responses have not previously been shown for any other HIV vaccine. Because this vaccine is scheduled for phase I clinical trials in 2016, understanding the mechanism of protective anti-HIV immunity induced by the vaccine is paramount. This research suggests this vaccine could have efficacy in humans.

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Third Award of $1,000