Identification and Characterization of a Novel Immune Response against AIDS Virus

Pathak, Reesab

After over three decades of HIV vaccine research, no suitable vaccine exists for clinical use today. As a result, a novel HIV vaccine modality is urgently needed. Recently, fifty percent of rhesus macaques vaccinated with recombinant Rhesus cytomegalovirus (RhCMV) strain 68-1 remarkably cleared viral infection with Simian Immunodeficiency Virus, an AIDS virus in primates. Here, deep sequencing technologies are used to determine MHC genetics of vaccinated macaques. Cells were then transfected with these single macaque MHC class I molecules to generate antigen presenting cells for use in novel ex vivo CD8+ T cell restriction assays. The data demonstrate that the major histocompatibility complex E (MHC-E) molecule universally restricts RhCMV vaccine-induced, SIV-specific CD8+ T cell responses. Using blocking peptide Rh67 VL9, these results are validated and the data indicate that every CMV-engendered, AIDS-specific, MHC-I restricted CD8+ T cell response is, indeed, MHC-E restricted. Finally, through ultra-deep, massively-parallel sequencing techniques, this work shows that MHC-E-restricted epitopes do not evade immune detection and that the CMV vaccine vector robustly targets nearly the entire proteome of the virus, causing only few sites of immune escape. Only one functional MHC-E molecule exists in humans, which is highly conserved with its rhesus homologue, is expressed in every tissue type, and is upregulated upon viral infection. Taken together, the findings of this study suggest that the CMV vaccine may hold efficacy against HIV when tested in humans.

Awards Won:
First Award of $5,000