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Poster presentation

HIV-1 Infections During Vaccine Trials: Identifying New Peptides for Differential Diagnosis of HIV-1 Infections in the Face of Vaccine-generated Antibodies

Surender Khurana*‡, James Needham and Hana Golding

Address: Div. of Viral Products, Center for Biologics Evaluation and Research (CBER), FDA, Bethesda, MD, USA 20892

Email: Surender Khurana* - khuranas@cber.FDA.gov

* Corresponding author ‡Presenting author

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Since 1987, more than 25,000 individuals have been immunized with 65 HIV preventive vaccines. Current candidate HIV-1 vaccines are complex products containing multiple HIV genes or proteins. As a result, high proportion of vaccinees score positive in licensed HIV diagnostic kits. This will have negative impact on vaccine trials that require early detection of breakthrough infections. For vaccinees it may contribute to range of social harms (jobs, insurance, blood donors). Therefore, it is important to design new tests that will discriminate between vaccine induced reactivity and true HIV infection. Our goals were to identify new HIV epitopes that: 1) Do not contain important neutralizing or CTL epitopes, 2) Recognized by antibodies early after HIV infection. 3) Highly conserved among HIV clades. Using Phage Display libraries constructed from whole HIV-1 genomes, combined with affinity selection with antibodies from early seroconvertors, we identified new immunodominant epitopes, in gp41 cytoplasmic tail and in p6 that fit the above criteria.

These peptides were used for development of new differential HIV-1 ELISA. To date, 100% specificity for gp41 and 99.4% with p6 peptide was observed with 1300 HIV seronegative samples. Analysis of 28 early HIV seroconversion panels showed that HIV-1 infection can be detected within 2 weeks following HIV-1 RNA detection by PCR. Testing of diverse HIV-1 clade panels from around the world (1660 samples) supports the utilization of our assay in detection of HIV-1 clade A, B, C, D, E, F and CRF infections. The assay sensitivity is 99.1%.

In recent testing of 2780 samples obtained from six HIV vaccine trials (with complex vaccine candidates (conducted by HVTN, DOD, Vaxgen & Vaccine Research Center), all samples from uninfected vaccines scored negative in our assay, while 46% samples were positive by commercial diagnostic kits. Importantly, our assay detected all 183 breakthrough HIV infections among these vaccinees, providing a strong proof-of-concept for utility of our EIA in diagnosis of true HIV infections in the face of vaccine generated antibodies.