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Universal biopanning strategy to identify epitopes associated with antibody-mediated vaccine protection against infectious pathogens

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Abstract

Identifying the immune correlates of protection is a key aspect of developing vaccines against infectious pathogens. We designed a universally applicable strategy to profile the antibody (Ab) repertoire of protected vaccine recipients, using recombinant phages encoding random peptide libraries. The novel approach, termed "protection-linked (PL) biopanning," uses subtractive biopanning and probes Ab paratopes of protected vaccinees ("winners") versus those with vaccine failure ("losers"). As proof-of-concept, we screened plasma samples from vaccinated macaques that had completely resisted multiple mucosal challenges with CCR5-tropic simian-human immunodeficiency viruses (SHIVs). The animals had been immunized with multimeric HIV-1 gp160 (Env), HIV-1 Tat, and SIV Gag-Pol particles. PL biopanning yielded a panel of approximately 100 recombinant phages that specifically reacted with Abs from "winners" and partially protected macaques but not Abs from "losers" or non-vaccinated, virus-challenged controls. Only about half of the phagotopes selected revealed amino acid homologies with HIV-1 Env (Env mimotopes). Expanding the sequence analysis to include non-Env immunogens revealed an unexpected additional humoral correlate of protection: the neutralizing epitope of HIV-1 Tat. Functional assays confirmed the induction of neutralizing anti-Tat Abs in macaques with full or partial protection but not in those with vaccine failure. Our data suggest that Tat should be included in multicomponent HIV-1 vaccines – and highlight the power of the new PL-biopanning strategy to identify Ab responses with significant association to vaccine protection, regardless of the mechanism(s) or targets of the protective Abs. PL biopanning is unbiased with regard to pathogens or disease model, making it a universal tool.

Biography

Ruprecht obtained her Ph.D. in Human Genetics from Columbia University, NY, and her M.D. from the University of Miami, FL. After training in internal medicine at UCLA and hematology-oncology at the Memorial Sloan-Kettering Cancer Center, NY, she joined the Dana-Farber Cancer Institute and Harvard Medical School, where she became a tenured professor of medicine. She recently joined the Texas Biomedical Research Institute/Southwest National Primate Research Center, where she plans to expand the AIDS Research Program. She is internationally known for her studies on AIDS vaccine development and lentiviral pathogenesis in primate models, especially mucosal virus transmission and its prevention.