Structure-based Vaccine Design of Human Rhinovirus: HIV Chimeras as Candidate AIDS Vaccines

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Our laboratory team has developed a system for generating combinatorial libraries of cold-causing human rhinoviruses (HRVs) that effectively display immunogenic peptide segments from a variety of pathogens. We have used this system to generate chimeric HRV-HIV-1 viruses displaying regions of the HIV-1 membrane-spanning protein gp41 that are part of the conserved and critical viral fusion machinery. We have generated chimeric HRVs displaying the so-called ELDKWA epitope of this region of gp41 that elicit immune responses able to broadly and potently cross-neutralize HIV-1 primary isolates, the first neutralizing responses reported for any ELDKWA-based immunogens. Ultimately, such immunogens might serve as valuable constituents in an AIDS vaccine.

Structural considerations for this vaccine engineering system will be discussed. We have obtained diffraction data at CHESS and BNL for several HRV:HIV-1 chimeras; structure determination is in progress. We are also investigating structures of chimeric virus complexed with anti-HIV neutralizing antibodies or Fab fragments. An important long-term goal is to identify three-dimensional correlates of immunogenicity and apply the knowledge to facilitate vaccine design and development using a structure-based approach.

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