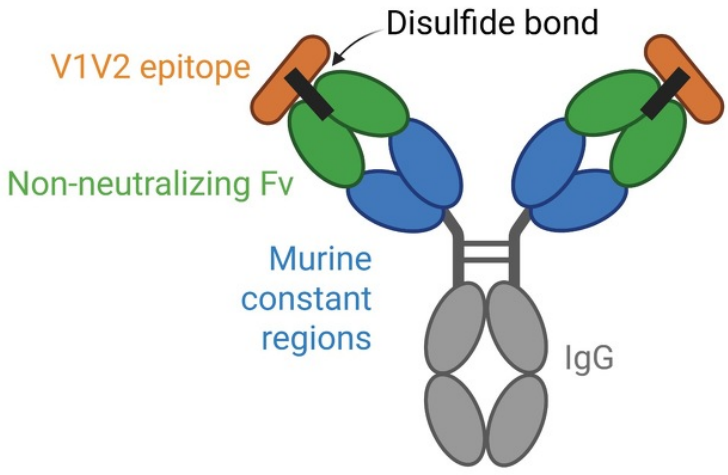
Innovative Immune Complex Approach for Generating a Broadly Neutralizing Antibody Response to HIV-1

A novel, innovative strategy for both treatment and prevention of HIV-1.

Technology

The Kong lab has developed a novel immune complex that can produce a broadly neutralizing antibody response to HIV-1 infection. This complex is designed to stabilize the highly variable V1/V2 domain of HIV-1 gp120 envelope glycoprotein, so the epitopes of known broadly neutralizing antibodies remain exposed. The inventors have generated a high-resolution cryo-EM structure of this complex, which is comprised of V1/V2 covalently linked to a bespoke non-neutralizing antibody. This work inspired the design of an immune complex variant that incorporates an additional disulfide bond at the V1/V2-antibody interface, further stabilizing the complex. Subsequent antigenicity assays confirmed that the immune complexes promote increased binding activity of known neutralizing antibodies and block recognition by non-neutralizing antibodies. Studies of mice, rabbit, and monkey immunization with these complexes are in progress.



Schematic of the novel immune complexes used to generate broadly neutralizing antibody response to HIV-1 infection.

Background

The HIV-1 gp120 envelope glycoprotein beta-barrel V1V2 domain is one of the most variable regions of the virus. Despite this heterogeneity, there are several known broadly neutralizing antibodies that target this domain. Until now, it has been challenging to design antigens that

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would stimulate an immune response to these broadly neutralizing epitopes because of the structural instability of this region. These epitopes are ideal candidates for a targeted immune response, as rare episodic antibodies against these epitopes have been shown to neutralize the majority of circulating HIV-1 strains, up to 80% of strains in some instances. The novel immune complex innovation described here leverages these optimal immunogenic epitopes while overcoming their structural complexities, thereby providing a reliable, broadly neutralizing immune response to HIV-1.

Development Stage

Researchers have successfully generated and purified immune complexes and have validated immunogenicity *in vitro*. Experiments to determine the immune response *in vivo* are underway.

Applications

- **Vaccination against HIV-1 infection:** Immunization with immune-complexes to generate a broadly neutralizing antibody response to protect from HIV-1 infection
- **Prophylactic or therapeutic treatment of HIV-1 infection:** Immune-complexes to generate an antibody response for preventing or treating HIV-1 infection
- **Diagnostic:** Detection of broadly neutralizing antibodies from patient samples using immune complexes

Advantages

- **Novel approach for targeting HIV-1 V1/V2 proteins:** V1/V2-targeting immunogens can be challenging to generate because of structural instability of these proteins
- **Broadly neutralizing antibody response:** Epitopes targeted by immune-complexes generate antibodies that can neutralize most circulating HIV-1 strains, up to 80% in some instances
- **Applicable to prevention and treatment of HIV-1 infection:** Immune complexes can be used for vaccination, treatment and diagnostic modalities of HIV-1

Intellectual Property

NYU has filed a provisional patent application covering composition and method of use.