Newly engineered peptide shows potential as long-acting anti-HIV drug

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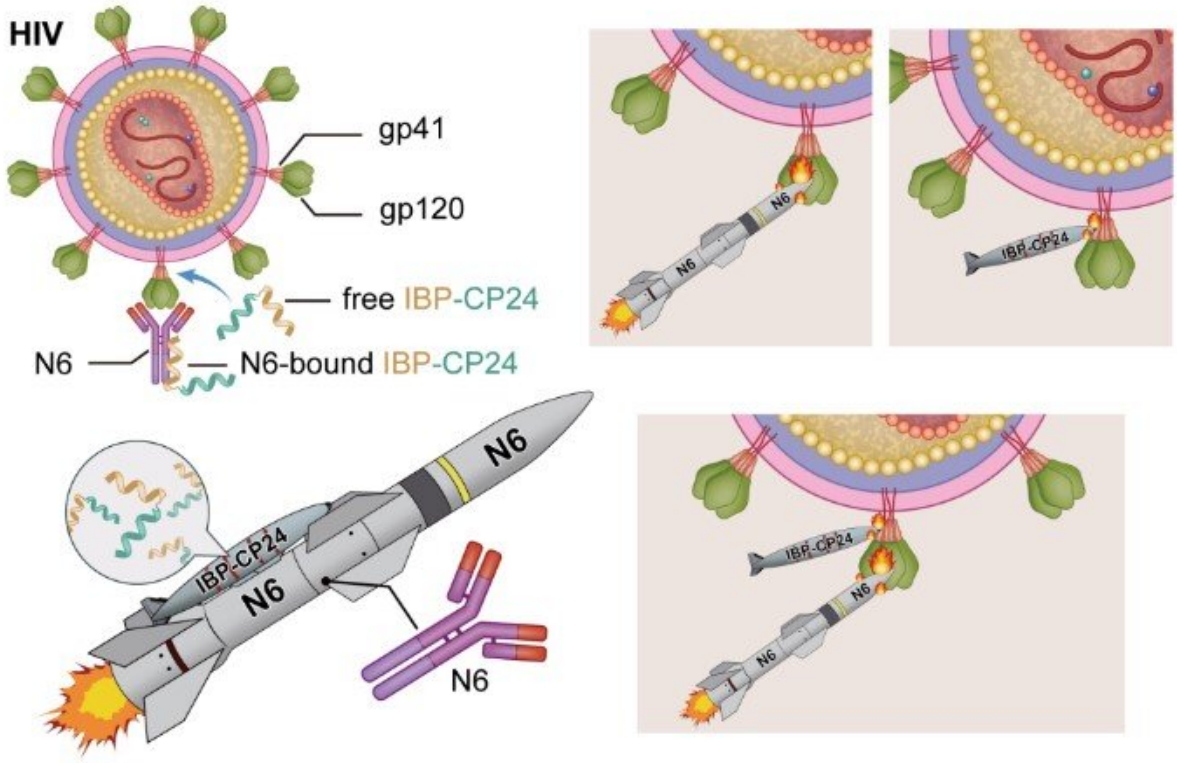

Anti-HIV-1 strategy of a long-acting fusion inhibitory peptide in combination with a broad neutralizing antibody (bNAb). The bNAb N6 may act as a biomissile for carrying a long-acting fusion inhibitory peptide IBP-CP24. N6 can directly hit HIV-1 by targeting gp120, while IBP-CP24 released from N6 can strike HIV-1 by targeting gp41, resulting in an effect of "a double-hit" by targeting both gp120 and gp41 on one virion (lower panel) or "one-stone-two-birds" by targeting gp120 on one virion and gp41 on another virion (upper panel). Therefore, combination of IBP-CP24 and N6 is expected to have synergistic anti-HIV-1 effect. Credit: Bi W, et al. (2019)

A newly engineered peptide called IBP-CP24 has the potential to be further developed as a long-acting anti-HIV drug that can be used alone or in combination with a broad neutralizing antibody for the treatment and prevention of HIV-1 infection, according to a study published December 5 in the open-access journal *PLOS Pathogens* by Lu Lu and Shibo Jiang of Fudan University and Lishan Su of the University of North Carolina at Chapel Hill, and colleagues. As reported in the study, IBP-CP24 exhibited a prolonged half-life as well as potent and broad anti-HIV-1 activity, even against drug-resistant strains.

Enfuvirtide is the first anti-HIV peptide drug approved by the U.S. Food and Drug Administration. However, its clinical application is limited because of its short half-life and the emergence of enfuvirtide-resistant HIV strains. In the new study, researchers developed a novel strategy to prolong the half-life of a short anti-HIV peptide called CP24 by fusing it to the human Immunoglobulin G (IgG) Fc-binding peptide (IBP).

IBP-CP24 inhibited a broad spectrum of HIV-1 strains, including those resistant to enfuvirtide. Most importantly, its half-life in the blood of rhesus monkeys was 46.1 h, approximately 26- and 14-fold longer than that of CP24 and enfuvirtide, respectively. IBP-CP24 intravenously administered in rhesus monkeys did not induce significant IBP-CP24-specific antibody response and showed no obvious toxicity. Mice pretreated with IBP-CP24 were protected from HIV-1 infection, and co-administration of IBP-CP24 and normal human IgG in mice with chronic HIV-1 infection resulted in a significant decrease in viruses in the bloodstream. Interestingly, the combined use of IBP-CP24 and a broad HIV neutralizing antibody showed a synergistic anti-HIV-1 effect, suggesting that this strategy may reduce the dose of the antibody and peptide and the cost of treatment.

More information: Bi W, Xu W, Cheng L, Xue J, Wang Q, Yu F, et al. (2019) IgG Fc-binding motif-conjugated HIV-1 fusion inhibitor exhibits improved potency and in vivo half-life: Potential application in combination with broad neutralizing antibodies. *PLoS Pathog* 15(12): e1008082. doi.org/10.1371/journal.ppat.1008082