Fusion Proteins as HIV-1 Entry Inhibitors

Summary (1024-character limit)
Novel fusion proteins with good stability and potency against HIV-1. These fusion proteins have good drug properties and potential as prophylactics or therapeutics against HIV-1 infection. Researchers at the NCI seek licensing for the development and commercialization of novel fusion proteins as therapeutics or prophylactics against HIV-1 infection.

NIH Reference Number
E-086-2015

Product Type
• Therapeutics

Keywords
• sCD4, HIV-1, antibody dependent cellular cytotoxicity (ADCC), Class II major histocompatibility complex (MHCII), fusion protein, Dimitrov

Collaboration Opportunity
This invention is available for licensing.

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Description of Technology
Soluble forms of human CD4 (sCD4) inhibit HIV-1 entry into immune cells. Different forms of sCD4 and their fusion proteins have been extensively studied as promising HIV-1 inhibitors – including in animal models and clinical trials. However, they have not been successful in human studies due to their transient efficacy. sCD4 is also known to interact with class II major histocompatibility complex (MHCII) and, at low concentrations, could enhance HIV-1 infectivity.

NCI researchers previously described a novel bispecific multivalent fusion protein called 4Dm2m which contains a single human CD4 domain (mD1.22) and a potent HIV-1 inhibitor (m36.4) (NIH Reference No. E-033-2013). mD1.22 is highly soluble and stable with good neutralizing activity without measurable interaction with MHCII. The NCI inventors have recently discovered new variants of 4Dm2m with increased stability and potency in mediating antibody dependent cellular cytotoxicity (ADCC) against
cells expressing the HIV-1 envelope glycoprotein. The newly identified variants also have increased half-lives in vivo and enhanced antibody binding.

Potential Commercial Applications
- Prophylactic or therapeutic against HIV-1 infection
- Rapid detection of HIV virus

Competitive Advantages
- Increased stability and half-life over previously identified fusion protein
- Enhanced potency in mediating ADCC against HIV-1 infected cells
- Continuous expression of high levels of these soluble receptors in vivo may overcome biggest challenge to efficacy in patients with HIV-1 infection

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Development Stage
- Pre-clinical (in vivo)

Publications
Chen W, et al. Improving the CH1-CK heterodimerization and pharmacokinetics of 4Dm2m, a novel potent CD4-antibody fusion protein against HIV-1. [PMID: 26963639]

Chen W, et al. Exceptionally potent and broadly cross-reactive, bispecific multivalent HIV-1 inhibitors based on single human CD4 and antibody domains. [PMID: 24198429]

Patent Status

Related Technologies
- E-103-2010 - Single domain CD4, HIV-1 Antibodies, and Fusion Proteins for treatment of HIV
- E-033-2013 - HIV-1 Therapeutic Inhibits Viral Entry
- E-203-2015
- E-210-2016

Therapeutic Area
- Infectious Diseases