

HIV-1 ENTRY INHIBITOR

SUMMARY

The National Cancer Institute's Nanobiology Program seeks parties to co-develop soluble forms of CD4 as potent HIV-1 therapeutics.

REFERENCE NUMBER

E-033-2013

PRODUCT TYPE

- Therapeutics

KEYWORDS

- HIV
- entry inhibitor
- CD4
- soluble expression
- MHCII

COLLABORATION OPPORTUNITY

This invention is available for licensing.

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DESCRIPTION OF TECHNOLOGY

Soluble forms (sCD4) of human CD4, the HIV-1 primary receptor, are potent HIV-1 entry inhibitors. Both four-domain (D1-4) and two-domain (D1D2) sCD4 and their fusion proteins have been tested as candidate therapeutics in animal models and in human clinical trials and were well tolerated by patients with no significant clinical or immunologic toxicities and exhibited significant inhibitory activities. However, their activities were transient and the virus rapidly rebound. Additionally, sCD4 is known to interact with the class II major histocompatibility complex (MHCII) and, at low concentrations, it could enhance the HIV-1 infectivity. Researchers at the National Cancer Institute's [Nanobiology Program](#) have generated a novel polypeptide comprising a single human CD4 domain (mD1.22) that is highly soluble, stable and shows significantly increased neutralizing activity without measurable interaction with MHCII. Due to these favorable properties, mD1.22 is highly promising for several applications:

- conjugated with cytotoxic molecules for eradication of HIV-infected cells;
- to generate multi-specific, multi-valent, HIV inhibitors with high neutralization potency and breadth, and relatively small molecular size;
- to generate nanobiosensors for rapid HIV detection; and
- to study the biological functions of CD4 in immune responses and HIV entry.

POTENTIAL COMMERCIAL APPLICATIONS

- As a prophylactic or an HIV therapeutic when conjugated with cytotoxic molecules
- Reagents for the rapid detection of HIV

COMPETITIVE ADVANTAGES

- Enhanced safety profile due to a lack of measurable interaction with MHCII
- Can be solubly expressed in *E. coli* with high yields leading to decreased production costs

INVENTOR(S)

Dimiter Dimitrov, Ph.D. (NCI)

DEVELOPMENT STAGE

- Discovery (Lead Identification)

PUBLICATIONS

- Chen W, et al. *J Virol.* 2011;85(18):9395-405. [PMID [21715496](#)]
- Chen W, et al. *Antiviral Res.* 2010;88(1):107-15. [PMID [20709110](#)]

PATENT STATUS

- **U.S. Filed:** US Application No. 61/791,885 filed 15 Mar 2013
- **Not Patented:** none

RELATED TECHNOLOGIES

- E-103-2010

THERAPEUTIC AREA

- Cancer/Neoplasm
- Infectious Diseases