

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, DHHS.

ACTION: Notice.

SUMMARY: The invention listed below is owned by an agency of the U.S. Government and is available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

ADDRESSES: Licensing information and copies of the U.S. patents and patent applications listed below may be obtained by contacting Michael Ambrose, Ph.D., at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804; telephone: 301/594-6565; fax: 301/402-0220; e-mail: ambrosem@mail.nih.gov. A signed Confidential Disclosure Agreement will be required to receive copies of any patent applications.

Efficient Inhibition of HIV-1 Viral Entry Through a Novel Fusion Protein Including CD4

James Arthos, Claudia Cicala, Anthony Fauci (NIAID).

U.S. Provisional Application No. 60/346,231 filed 25 Oct 2001 (DHHS Reference No. E-337-2001/0-US-01); PCT Application No. PCT/US02/34393 filed 24 Oct 2002 (DHHS Reference No. E-337-2001/0-PCT-01).

This invention relates to CD4 fusion proteins for use in the treatment of an immunodeficiency virus infection such as human immunodeficiency virus (HIV). These polypeptides have been shown by the inventors to inhibit the entry of primary isolates of HIV-1 into CD4+ T cells by targeting the gp120 subunit of the HIV-1 envelope. The invention claims recombinant polypeptides comprising a CD4 polypeptide ligated at its C-terminus with a portion of a human immunoglobulin comprising a hinge region and two constant domains of an immunoglobulin heavy chain. The portion of the IgG is fused at its C-terminus with a polypeptide comprising

a tailpiece from the C terminus of the heavy chain of an IgA antibody. This protein is very large (greater than 800 kilodaltons), which may contribute to its ability to inhibit entry of primary isolates of HIV-1 into T cells. It presents twelve gp120 binding domains (D1D2) and can bind at least ten gp120s simultaneously. The inventors have shown that the construct efficiently neutralizes primary isolates from different HIV subgroups. Also claimed are use of the construct as a component of a vaccine and as a diagnostic.

Identification of New Small RNAs and ORFs

Susan Gottesman (NCI), Gisela Storz (NICHHD), Karen Wassarman (NICHHD), Francis Repoila (NCI), Carsten Rosenow (EM).

U.S. Provisional Application No. 60/266,402 filed 01 Feb 2001 (DHHS Reference No. E-072-2001/0-US-01); PCT Application No. PCT/US02/03147 filed 31 Jan 2002 (DHHS Reference No. E-072-2001/0-PCT-02); U.S. Patent Application filed 25 Jul 2003 (DHHS Reference No. E-072-2001/0-US-03).

The inventors have isolated a number of previously unknown sRNAs found in *E. coli*. Previous scientific publications by the inventors and others regarding sRNAs have shown these sRNAs to serve important regulatory roles in the cell, such as regulators of virulence and survival in host cells. Prediction of the presence of genes encoding sRNAs was accomplished by combining sequence information from highly conserved intergenic regions with information about the expected transcription of neighboring genes. Microarray analysis also was used to identify likely candidates. Northern blot analyses were then carried out to demonstrate the presence of the sRNAs. Three of the sRNAs claimed in the invention regulate (candidates 12 and 14, negatively and candidate 31, positively) expression of RpoS, a major transcription factor in bacteria that is important in many pathogens because it regulates (amongst other things) virulence. The inventors' data show that these sRNAs are highly conserved among closely related bacterial species, including *Salmonella* and *Klebsiella*, presenting a unique opportunity to develop both specific and broad-based antibiotic therapeutics. The invention contemplates a number of uses for the sRNAs, including, but not limited to, inhibition by antisense, manipulation of gene expression, and possible vaccine candidates.

A Novel Chimeric Protein for Prevention and Treatment of HIV Infection

Edward A. Berger (NIAID), Christie M. Del Castillo.

U.S. Provisional Application No. 60/124,681 filed 16 Mar 1999 (DHHS Reference No. E-039-1999/0-US-01); PCT Application No. PCT/US00/06946 filed 16 Mar 2000 (DHHS Reference No. E-039-1999/0-PCT-02); U.S. Patent Application No. 09/936,702 filed 13 Sep 2001 (DHHS Reference No. E-039-1999/0-US-03).

This invention relates to bispecific fusion proteins effective in viral neutralization. Specifically, the invention is a genetically engineered chimeric protein containing a soluble extracellular region of human CD4 attached via a flexible polypeptide linker to a single chain human monoclonal antibody directed against a CD4-induced, highly conserved HIV gp120 determinant involved in coreceptor interaction. Binding of the sCD4 moiety to gp120 induces a conformational change that enables the antibody moiety to bind, thereby blocking Env function and virus entry. This novel bispecific protein displays neutralizing activity against genetically diverse primary HIV-1 isolates, with potency at least 10-fold greater than the best described HIV-1 neutralizing monoclonal antibodies. The agent has considerable potential for prevention of HIV-1 infection, both as a topical microbicide and as a systemic agent to protect during and after acute exposure (e.g. vertical transmission, post-exposure prophylaxis). It also has potential utility for treatment of chronic infection. Such proteins, nucleic acid molecules encoding them, and their production and use in preventing or treating viral infections are claimed.

Novel Antimalarial Compounds, Methods of Synthesis Thereof, Pharmaceutical Compositions Comprising Same, and Methods of Using Same for Treatment and Prevention of Malaria

Michael R. Boyd (NCI), Gerhard Bringmann (EM), Sven Harmsen (EM), Roland Gotz (EM), T. Ross Kelly (EM), Matthias Wenzel (EM), Guido Francois (EM), J. D. Phillipson (EM), Laurent A. Assi (EM), Christopher Schneider (EM).

U.S. Patent 5,639,761 issued on 17 Jun 1997 (DHHS Reference No. E-090-1994/0-US-01); U.S. Patent 6,627,641 issued on 30 Sep 2003 (DHHS Reference No. E-090-1994/0-US-07); U.S. Patent 5,552,550 issued on 03 Sep 1996 (DHHS Reference No. E-