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 (NICHD), Karen Wassarman (NICHD), 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–

200–1994/0–US–01); U.S. Patent 5,763,613 issued on 09 Jun 1998 (DHHS Reference No. E–200–1994/0–US–02); U.S. Patent 6,140,339 issued on 31 Oct 2000 (DHHS Reference No. E–200–1994/2–US–01); U.S. Patent 6,331,630 issued on 18 Dec 2001 (DHHS Reference No. E–200–1994/2–US–08); U.S. Patent 5,571,919 issued on 05 Nov 1996 (DHHS Reference No. E–201–1994/0–US–01); U.S. Patent 5,789,594 issued on 04 Aug 1998 (DHHS Reference No. E–201–1994/0–US–02); U.S. Patent 5,578,729 issued on 26 Nov 1996 (DHHS Reference No. E–201–1994/1–US–01); U.S. Patent 5,786,482 issued on 28 Jul 1998 (DHHS Reference No. E–201–1994/1–US–03).

According to data recently reported by the World Health Organization (WHO), the death rate from malaria exceeds one million individuals per year. The Public Health Service seeks exclusive or non-exclusive licensee(s) to develop and commercialize the technology claimed within the portfolio of U.S. patents issued and pending, and corresponding international patents issued and pending. These patents and pending applications claim an exceptionally broad universe of novel naphthylisoquinoline alkaloid compounds, and methods of total synthesis thereof. Representative examples of these compounds have been shown to have potent in vitro activity against malaria parasites, including parasites that are highly resistant to available antimalarial drugs.

Representative examples have also been shown to have potent in vivo activity against malaria parasites in animal models. Pharmaceutical compositions comprising these compounds, as well as methods of using the compounds to treat or prevent a malarial infection of a host, are claimed. The relative structural simplicity of this class of compounds, and the ready synthetic access thereto, provide unprecedented opportunities for structure-activity relationship (SAR), lead-optimization and antimalarial drug development. The technology is further described in the following publications: J. Nat Prod. 1997 Jul.;60(7):677–83 and Bioorg. Med. Chem. Lett. 1998 Jul.;8(13): 1729–34.

Antimicrobial Magainin Peptides

Michael A. Zasloff, Hao-Chia Chen, Judith H. Brown, John L. Morell, Charng-Ming Huang (NICHD).

U.S. Patent 4,810,777 issued on 07 Mar 1989 (DHHS Reference No. E–145–1987/0–US–01); U.S. Patent 5,567,681 issued on 22 Oct 1996 (DHHS Reference No. E–145–1987/2–US–03); U.S. Patent 5,643,876 issued on 01 Jul 1997 (DHHS Reference No. E–145–1987/1–US–03); U.S. Patent 5,221,732 issued on 22 Jun 1993 (DHHS Reference No. E–217–1988/0–US–01).

First isolated from the skin of the African clawed frog Xenopus laevis, magainin peptides have been shown by the inventors to have broad-spectrum antimicrobial properties. Both synthetic and natural magainin peptides are active against many species of bacteria and fungi and induce osmotic lysis of protozoa. Magainin peptides are water soluble, nonhemolytic at effective antimicrobial concentrations, have molecular weights of 2500 or less and are amphiphilic. Compositions and methods for their use are claimed in the patents. These inventions are available for nonexclusive or exclusive licensing. The inventions are further described in Zasloff *et al.*, P.N.A.S. USA 1987 Aug.; 84(15):5449–53; Marion *et al.*, FEBS Lett. 1988 Jan.18;227(1):21–6; Soravia *et al.*, FEBS Lett. 1988 Feb. 15;228(2):337–40; Westerhoff *et al.*, P.N.A.S. USA 1989 Sep.; 86(17):6597–601; and Gwadz *et al.*, Infect. Immun. 1989 Sep.; 57(9):2628–33.

Dated: October 24, 2003.

Steven M. Ferguson,

Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.

[FR Doc. 03–28060 Filed 11–6–03; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Cancer Institute; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Cancer Institute Initial Review Group, Subcommittee C—Basic & Preclinical.

Date: December 9–10, 2003.

Time: 7 p.m. to 6 p.m.

Agenda: To review and evaluate grant applications.

Place: Holiday Inn Select Bethesda, 8120 Wisconsin Ave, Bethesda, MD 20814.

Contact Person: Michael B. Small, PhD., Scientific Review Administrator, Research Programs Review Branch, Division of Extramural Activities, National Cancer Institute, National Institutes of Health, 6116 Executive Boulevard, Room 8127, Bethesda, MD 20892, 301–402–0996, *smallm@mail.nih.gov.*

(Catalogue of Federal Domestic Assistance Program Nos. 93.392, Cancer Construction; 93.393, Cancer Cause and Prevention Research; 93.394, Cancer Detection and Diagnosis Research; 93.395, Cancer Treatment Research; 93.396, Cancer Biology Research; 93.397, Cancer Centers Support; 93.398, Cancer Research Manpower; 93.399, Cancer Control, National Institutes of Health, HHS)

Dated: October 30, 2003.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 03–28033 Filed 11–6–03; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Center for Research Resources; Notice of Closed Meetings

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meetings.

The meetings will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Center for Research Resources Special Emphasis Panel Clinical Research.

Date: November 12–13, 2003.

Time: November 12, 2003, 7:45 a.m. to Adjournment.

Agenda: To review and evaluate grant applications.

Place: University Place, 850 West Michigan Street, Indianapolis, IN 46202.

Contact Person: Marc Rigas, PhD., Scientific Review Administrator, National Center For Research Resources, or, National Institutes of Health, 6701 Democracy Blvd., 1 Democracy Plaza, rm 1080, MSC 4874,