

2. PHS Grants Policy Statement, and  
3. OMB Circular A-21, Cost  
Principles for Educational Institutions.

#### L. Objective Review Process

Applications meeting eligibility requirements that are complete, responsive, and conform to this program announcement will be reviewed by an Objective Review Committee (ORC) in accordance with IHS objective review procedures. The objective review process ensures a nationwide competition for limited funding. The ORC will be comprised of IHS (40% or less) and other federal or non-federal individuals (60% or more) with appropriate expertise. The ORC will review each application against established criteria. Based upon the evaluation criteria, the reviewers will assign a numerical score to each application, which will be used in making the final funding decision. Approved applications scoring less than 60 points will not be considered for funding.

#### M. Results of the Review

The results of the objective review are forwarded to the Director, Office of Management Support (OMS), for final review and approval. The Director, OMS, will also consider the recommendations from the Division of Health Professions Support and the Grants Management Branch. Applicants are notified in writing on or about August 3, 1998. A Notice of Grant Award will be issued to successful applicants. Unsuccessful applicants are notified in writing of disapproval. A brief explanation of the reasons the application was not approved is provided with the name of the IHS official to contact if more information is desired.

Dated: April 1, 1998.

**Michael H. Trujillo,**

Assistant Surgeon General, Acting Director.

[FR Doc. 98-9104 Filed 4-7-98; 8:45 am]

BILLING CODE 4160-16-M

## 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 inventions listed below are owned by agencies of the U.S. Government and are 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. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804; telephone: 301/496-7057; fax: 301/402-0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

#### A Human Cell Line Which Constitutively Expresses the Nonstructural (NS) Proteins of Hepatitis C Virus

G Sherman, S Feinstone (FDA)  
DHHS Reference No. E-012-98/0  
Licensing Contact: Carol Salata, 301/  
496-7735 ext. 232

Currently there are no good animal models or tissue culture systems which can be used in assaying compounds directed against HCV. A cell line has been developed which may represent a valuable tool in the identification of potential therapeutic agents against hepatitis C. This permanent human cell line contains an expression vector which directs cells to synthesize 5 nonstructural (NS) hepatitis C proteins: NS3, NS4a, NS4b, NS5a, and NS5b. Two of these proteins provide enzymatic activities crucial to virus replication (NS3: protease, helicase; NS5b, RNA polymerase). The cell line will permit the evaluation of antivirals directed against these enzymes.

#### Plasmodium Falciparum Gene Linked to Chloroquine Resistance in Human Malaria

TE Wellem, X-Z Su (NIAID)  
Serial No. 60/058,895 filed 15 Sep 97  
Licensing Contact: Carol Salata, 301/  
496-7735 ext. 232

Malaria infects over 200 million people annually worldwide, causing at least one million deaths yearly. Particularly affected areas of the world include Africa, Asia, the Indian subcontinent and South America. Malaria is caused by systemic infections with the parasite *Plasmodium* which infects blood and other tissues. Of the four species of *Plasmodium* that can infect humans, *P. falciparum* is the most deadly. Therapeutic and preventive approaches to control malaria include the use of drugs, particularly drugs that are chemically related to quinine, and

the attempted development of vaccines that confer immunological resistance to infection.

Chloroquine, once a first-line drug for control of malaria, now fails frequently against *P. falciparum*. This invention relates to methods and reagents for diagnosis of chloroquine-resistant malarial infections caused by *P. falciparum*, and the development of new antimalarial drugs against these infections. These diagnostics are based on a unique and heretofore unknown gene and its protein product linked to chloroquine resistance in *P. falciparum* malaria. Because of the worldwide incidence of chloroquine-resistant *P. falciparum*, there is a need for diagnostic methods for detecting chloroquine-resistant malaria, thus allowing such infected individuals to be treated with alternative drugs. Furthermore, there is a need to design and/or screen for new antimalarial agent that can take the place of chloroquine. Use of alternative drugs may prevent further spread of chloroquine-resistant *P. falciparum* in infected individuals.

#### Phage Display of Intact Domains at High Copy Number

AC Steven (NIAMS)

Serial No. 08/837,301 filed 11 Apr 97  
Licensing Contact: Carol Salata, 301/  
496-7735 ext. 232

Filamentous phage-based display systems have found widespread use in molecular biology, including many immunologic applications such as antigen presentation and the immunoisolation of desired recombinants by "biopanning". The present invention relates to a phage display system in which the molecules to be displayed (i.e., molecules of interest) are covalently connected to dispensable capsid polypeptides such as SOC (small outer capsid) and HOC (highly antigenic outer capsid) polypeptides that are, in turn, bound to a surface lattice protein, such as those on the surface of a virion or polyhead. Polyheads are tubular capsid variants containing much longer numbers of the surface lattice protein. Molecules of interest may be displayed in various ways. For example, a chimeric polypeptide that includes a dispensable polypeptide and a polypeptide of interest can be expressed in *Escherichia coli*, purified, and then bound *in vitro* to separately isolated surface lattice proteins. The surface lattice proteins can be those on the surface of a capsid or polyhead from which the wild type dispensable polypeptides have been deleted. Similarly, a chimera that contains a

dispensable polypeptide and a synthetic molecule of interest can be prepared *in vitro* and bound to surface lattice proteins. In another embodiment, a positive selection vector forces integration of a gene that encodes a dispensable polypeptide and a polypeptide of interest into the genome of a phage from which the wild type dispensable polypeptide is deleted. For example, a modified *soc* gene can be integrated into a *soc*-deleted T4 genome, leading to *in vivo* binding of the display molecule on progeny virions. More than one type of dispensable polypeptide can be used as part of the chimera for displaying one or more molecules of interest. For example, the surface lattice proteins of a phage may be bound to a chimera that contains SOC and a chimera that contains HOC.

The display system has been successfully demonstrated for three molecules of interest that vary in their length and character: (1) a tetrapeptide; (2) the 43 amino acid residue V3 loop domain of gp120, the human immunodeficiency virus type-1 (HIV-1) envelope glycoprotein; and (3) poliovirus VP1 capsid protein (312 residues).

#### **Ultrasound-Hall Effect Imaging System and Method**

H Wen (NHLBI)

DHHS Reference No. E-067-96/0; PCT/US97/11272 filed 03 Jul 97 Licensing Contact: John Fahner-Vihtelic, 301/496-7735 ext. 270

The present application provides for a new ultrasound-based imaging modality that is based on the interaction among a static magnetic field and conductive moieties in the imaged sample under electrical excitation. The application also provides a new ultrasound-based imaging modality that provides a contrast mechanism which reflects the conductivity distribution of the medium being imaged. The disclosed methods and system are advantageous over other ultrasonic imaging systems in the following aspects: it provides a method which is not limited to contrast based solely on acoustic properties; it dispenses with acoustic beam excitation, and therefore is suitable for fast 2D and 3D image formation with wide angle signal reception. A working prototype system is in testing and the present invention is suitable for development into commercial computed imaging products for biomedical imaging and industrial non-destructive testing.

#### **Multideterminant Peptide Antigens That Stimulate Helper T Lymphocyte Response to HIV in a Range of Human Subjects**

JA Berzofsky, JD Ahlers, PL Nara, M Shirai, CD Pendleton (NCI) Serial No. 08/060,988 filed 14 May 93; PCT/US94/05142 filed 13 May 94  
Licensing Contact: Robert Benson, 301/496-7056 ext. 267

A vaccine for the prevention and/or treatment of HIV infection would ideally elicit a response in a broad range of the population. It would also have the capability of inducing high titered neutralizing antibodies, cytotoxic T lymphocytes, and helper T cells specific for HIV-1 gp 160 envelope protein. A vaccine based on synthetic or recombinant peptides has been developed which elicits these responses while avoiding the potential safety risks of live or killed viruses. Unlike previously developed vaccines this invention avoids those regions of gp 160 which may contribute to acceleration of infection or the development of immune deficiency. This invention provides peptides up to 44 amino acid residues long that stimulate helper T-cell response to HIV in a range of human subjects. Six multideterminant regions have been identified in which overlapping peptides are recognized by mice of either three or all four MHC types. Four of the six regions have sequences relatively conserved among HIV-1 isolates. These multideterminant cluster peptides are recognized by T cells from humans of multiple HLA types, and have been found in a phase I clinical trial to elicit neutralizing antibodies, cytotoxic T cells, and helper T cells in at least some of the human subjects.

#### **Mucosal Cytotoxic T Lymphocyte Responses**

J. Berzofsky, I Belyakov, M Derby, B Kelsall, W Strober (NCI)  
DHHS Reference No. E-268-97/1 (incorporating USSN 60/058,523) filed 17 Feb 98 (priority to 11 July 97)  
Licensing Contact: Robert Benson, 301-496-7056 ext. 267

This invention is the discovery that intrarectal (IR) administration of a peptide antigen can induce an antigen-specific, protective CTL response in the mucosal and systemic immune system. The CTL response is much greater than occurs with intranasal administration. The CTL response is enhanced by co-administration of a mucosal adjuvant such as cholera toxin, and is further enhanced by IR administration of interleukin 12 (IL-12). IR administration of an HIV-1 peptide vaccine protected

mice against an IR challenge with a recombinant vaccinia virus expressing HIV gp160. This invention provides an approach to the use of peptide vaccines that protect against mucosal infection, especially for HIV. The invention is further described in Proc. Natl. Acad. Sci. USA, Vol. 95, pp. 1709-1714, 1998.

Dated: March 31, 1998.

**Barbara M. McGarey,**

*Deputy Director, Office of Technology Transfer.*

[FR Doc. 98-9177 Filed 4-7-98; 8:45 am]

BILLING CODE 4140-01-M

## **DEPARTMENT OF HEALTH AND HUMAN SERVICES**

### **National Institutes of Health**

#### **Center for Scientific Review; 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 Center for Scientific Review Special Emphasis Panel (SEP) meetings:

*Purpose/Agenda:* To review individual grant applications.

*Name of SEP:* Behavioral and Neurosciences.

*Date:* April 8, 1998.

*Time:* 4:00 p.m.

*Place:* NIH, Rockledge 2, Room 5190, Telephone Conference.

*Contact Person:* Dr. Herman Teitelbaum, Scientific Review Administrator, 6701 Rockledge Drive, Room 5190, Bethesda, Maryland 20892, (301) 435-1254.

*Name of SEP:* Microbiological and Immunological Sciences.

*Date:* April 14, 1998.

*Time:* 1:00 p.m.

*Place:* NIH, Rockledge 2, Room 4194, Telephone Conference.

*Contact Person:* Dr. Jean Hickman, Scientific Review Administrator, 6701 Rockledge Drive, Room 4194, Bethesda, Maryland 20892, (301) 435-1146.

*Name of SEP:* Biological and Physiological Sciences.

*Date:* April 14, 1998.

*Time:* 10:00 a.m.

*Place:* NIH, Rockledge 2, Room 5202, Telephone Conference.

*Contact Person:* Dr. Anita Sostek Miller, Scientific Review Administrator, 6701 Rockledge Drive, Room 5202, Bethesda, Maryland 20892, (301) 435-1260.

*Name of SEP:* Biological and Physiological Sciences.

*Date:* April 14, 1998.

*Time:* 1:00 p.m.

*Place:* NIH, Rockledge 2, Room 4142, Telephone Conference.

*Contact Person:* Dr. Edmund Copeland, Scientific Review Administrator, 6701 Rockledge Drive, Room 4142, Bethesda, Maryland 20892, (301) 435-1715.