Type of respondent	Number of respondents	Responses per respondent	Total number of responses	Burden per responses (minutes)	Total burden hours
Applicants	1,850	1	1,850	12	370
Lenders	9	206	1,854	30	927
Total	1,859		3,704		1,297

Send comments to Susan G. Queen, Ph.D., HRSA Reports Clearance Officer, Room 14–33, Parklawn Building, 5600 Fishers Lane, Rockville, MD 20857. Written comments should be received within 60 days of this notice.

Dated: May 25, 2001.

Jane M. Harrison,

Director, Division, of Policy Review and Coordination.

[FR Doc. 01–13850 Filed 6–1–01; 8:45 am]

BILLING CODE 4160–15–P

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.

PRAC & PRAC–Y: Small Nuclear Proteins Found in Prostate and Colon Cancer, and Uses Thereof

Ira Pastan et al. (NCI)

DHHS Reference No. E–053–01/0, filed 09 Apr 2001

Licensing Contact: Richard Rodriguez; 301/496–7056, ext. 287; e-mail: rodrigur@od.nih.gov

Prostate cancer is the most commonly diagnosed cancer and the second leading cause of cancer death in males in the United States. Currently, there are no curative therapies available for this cancer and therefore, novel approaches are needed to treat this disease. The present invention claims a small, nuclear protein, PRAC (Prostate/Rectum And Colon Protein) that could be used to diagnose and/or treat prostate or colon cancers. In conjunction with the composition of matter claims, defined methods of use might include: (1) Immunogenic fragments to elicit T cell responses against cells that express PRAC; (2) gene therapy applications through the use of appropriate expression vectors containing the nucleic acid sequences of PRAC; (3) detection and potential staging of cancers expressing PRAC. These disclosed technologies could provide new and exciting methodologies to treat prostate and/or colon cancer.

Biologically Active Macrolides, Compositions and Uses Thereof

Michael R. Boyd (NCI), Kirk R. Gustafson (NCI), and Charles L. Cantrell (USDA)

DHHS Reference No. E–203–00/0, filed 24 Jul 2000

Licensing Contact: Elaine White; 301/496–7056, ext. 282; e-mail: gesee@od.nih.gov

The current invention embodies the identification of a novel class of potent vacuolar-type (H+)-ATPase-inhibitory compounds. Vacuolar-type (H+)-ATPases are present in many tissues and cells of the body and are involved in the maintenance of various physiological functions. The modification of these functions, via inhibition of vacuolar-type (H+)-ATPases, may represent an effective means of treating various disease states, including Alzheimer's disease, glaucoma, and osteoporosis. In addition, these inhibitors may also be of particular value for use against cancer, as vacuolar-type (H+)-ATPases have been implicated in processes relating to cellular proliferation, angiogenesis, tumor cell invasiveness, metastasis, and drug resistance.

Dated: May 24, 2001.

Jack Spiegel,

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

[FR Doc. 01–13886 Filed 6–1–01; 8:45 am]

BILLING CODE 4140–01–P

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 contacting Peter A. Soukas, J.D., at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804; telephone: 301/496–7056 ext. 268; fax: 301/402–0220; e-mail: soukasp@od.nih.gov. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Identification of New Small RNAs and ORFs

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

DHHS Reference No. E–072–01/0, filed 01 Feb 2001

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.

LL–37 Is an Immunostimulant

Oleg Chertov (NCI), Joost Oppenheim (NCI), De Yang (NCI), Qian Chen (NCI), Ji Wang (NCI), Mark Anderson (EM), Joseph Wooters (EM)

Serial No. 60/233,983, filed 21 Sep 2000

This invention relates to use of an antimicrobial peptide as a vaccine adjuvant. LL–37 is the cleaved antimicrobial 37-residue C-terminal peptide of hCAP18, the only identified member in humans of a family of proteins called cathelicidins. LL–37/hCAP18 is produced by neutrophils and various epithelial cells. LL–37 is well known as an antimicrobial peptide. However, although antimicrobial peptides have generally been considered to contribute to host innate antimicrobial defense, some of them may also contribute to adaptive immunity against microbial infection. The inventors have shown that LL–37 utilizes formyl peptide receptor-like 1 (FPLR1) as a receptor to activate human neutrophils, monocytes, and T cells. Since leukocytes participate in both innate and adaptive immunity, the fact that LL–37 can chemoattract human leukocytes may provide one additional mechanism by which LL–37 can contribute to host defense against microbial invasion, by participating in the recruitment of leukocytes to sites of infection. The invention claims methods of enhancing immune responses through the administration of LL–37 alone, in conjunction with a vaccine, and methods of treating autoimmune diseases. The invention is further described in Chertov et. al., ''LL–37, the neutrophil granule-and epithelial cell-derived cathelicidin, utilizes formyl peptide receptor-like 1 (FPRL1) as a receptor to chemoattract human peripheral blood neutrophils, monocytes, and T cells,'' J Exp. Med. 2000 Oct 2;192(7):1069–74.

Vibrio cholerae O139 Conjugate Vaccines

Shousun Szu, Zuzana Kossaczka, John Robbins (NICHD)

DHHS Reference No. E–274–00/0; PCT/US00/24119, filed 01 Sep 2000

Cholera remains an important public health problem. Epidemic cholera is caused by two Vibrio cholerae serotypes O1 and O139. The disease is spread through contaminated water. According to information reported to the World Health Organization in 1999, nearly 8,500 people died and another 223,000 were sickened with cholera worldwide. This invention is a polysaccharide-protein conjugate vaccine to prevent and treat infection by Vibrio cholerae O139 comprising the capsular polysaccharide (CPS) of V. cholerae O139 conjugated through a dicarboxylic acid dihydrazide linker to a mutant diphtheria toxin carrier. In addition to the conjugation methods, also claimed in the invention are methods of immunization against V. cholerae O139 using the conjugates of the invention. The inventors have shown that the conjugates of the invention elicited in mice high levels of serum antibodies to CPS, a surface antigen of Vibrio cholerae O139, that have vibriocidal activity. Clinical trials of the two most immunogenic conjugates have been planned by the inventors. This invention is further described in Infection and Immunity 68(9), 5037–5043, Sept. 2000.

A Novel Chimeric Protein for Prevention and Treatment of HIV Infection

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

Serial No. 60/124,681, filed 16 Mar 1999 and PCT/US00/06946, filed 16 Mar 2000

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.

Beta2-Microglobulin Fusion Proteins and High Affinity Variants

RK Ribaudo, M Shields (NCI)

Serial No. 09/719,243, filed 07 Dec 2000 (with priority back to Serial No. 60/088,813, filed 10 Jun 1998) and European Patent Application Number 99928376.5

This invention concerns fusion proteins comprising b2-microglobulin (b2M), a component of the MHC–1 complex, and immunologically active proteins such as the co-stimulatory molecule B7. The fusion proteins, and nucleic acids encoding them, have broad utility activating Cytotoxic T Lymphocytes (CTLs) against viruses and tumors. The fusion proteins locate to the surface of MHC–1 expressing cells. They may be used as adjuvants to enhance the efficacy of MHC–1 binding peptides, from viruses or cancer antigens, as vaccines. The fusion proteins can be used, in vivo or ex vivo, to enhance the immunogenicity of cancer cells to cause their destruction by the immune system. B7-b2M is as effective at co-stimulating T-cells in comparison to anti-CD28 monoclonal antibodies, whereas wild-type b2M is ineffective at co-stimulating T-cells. In addition, B7-b2M induces better recognition and killing of tumor cell lines compared to wild-type b2M. Another aspect of the invention is a mutant human b2M that binds MHC–1 with higher affinity than wild-type b2M. It can be used in place of wild-type b2M, including in the fusion proteins, to greater effect.

Virus-Like Particles as Unlinked Adjuvants

John Schiller, Bryce Chackerian, Joseph Lee, Douglas Lowy (NCI)

Serial No. 60/219,763, filed 20 Jul 2000

This invention claims immunostimulating or vaccine compositions in which non-infectious virus-like particles (VLPs) serve as unlinked adjuvants. Co-administration of VLPs with an antigen enhances induction of high titer IgG antibodies to self or foreign antigens and promotes T cell responses to foreign antigens. The VLP-target antigen combination can be administered alone or with a traditional adjuvant. The VLPs of the current invention are contemplated to comprise capsid protein(s) of a virus assembled into a shell resembling a virion, but not containing pathogenic viral DNA or RNA. The VLPs are unlinked, rather than physically linked to the antigen because this may reduce the manufacturing complexity of the vaccine. Unlinked VLP adjuvants, for example papillomavirus VLPs, of the invention have a number of advantages: (1) They are non-inflammatory in humans, (2) are potent at amplifying IgG antibody responses to self antigens, (3) induce a pronounced Th1 type of T cell response, and (4) may provide two-fold protection, against the virus corresponding to the VLP type, as well as against the disease associated with the other component in the VLP-target antigen combination.

Peptides That Stabilize Protein Antigens and Enhance Presentation to CD8+ T Cells

Roger Kurlander, Elizabeth Chao, Janet Fields (CC)

Serial No. 60/169,227, filed 06 Dec 1999 and PCT/US00/33027, filed 12 Dec 2000

This invention relates to compositions and methods for stabilizing an antigen against proteolytic degradation and enhancing its presentation to CD8+ cells. The invention claims ''fusion agents,'' isolated molecules comprising a hydrophobic peptide joined to an epitope to which a CD8+ T cell response is desired. Also claimed in the invention are the nucleic acid sequences that encode the fusion agents. Recently, there has been great interest in developing vaccines to induce protective CD8+ T cell responses, however, there are practical obstacles to this goal. Although purified antigenic peptides are effectively presented in vitro, introduced in a purified form they often do not stimulate effective T cell responses in vivo because the antigens are insufficiently immunogenic and too easily degraded. Adjuvants or infectious ''carriers'' often can enhance these immune responses, however, these added agents can cause unacceptable local or systemic side effects. The present invention increases antigen stability and promotes in vivo responses in the absence of an adjuvant or active infection.

The invention describes three variants of lemA, an antigen recognized by CD8+ cells in mice infected with Listeria monocytogenes. The antigenic and stabilizing properties of lemA can be accounted for by the covalent association of the immunogenic aminoterminal hexapeptide with the protease resistant scaffolding provided by amino acids 7 to 33 of the lemA sequence (lemA(7–33)). Variants t-lemA, and s-lemA bearing an antigenic sequence immediately preceding lemA(7–33), and lemS containing an immunogenic sequence immediately after lemA(7–33), each induce a CD8+ T cell response and protect the crucial immunogenic oligopeptide from protease degradation. The site of antigen insertion relative to lemA(7–33) can influence antigen processing by preferentially promoting processing either in the cytoplasm or endosomal compartment. Therefore, several embodiments of the invention involve the construction of antigen processing protein molecules and their methods of use. Alternatively, a DNA sequence coding lemA(7–33) may be inserted at an appropriate site to enhance the immunogenicity of the antigenic element coded by a DNA vaccine. In sum, this invention is an attractive, nontoxic alternative to protein/adjuvant combinations in eliciting CD8 responses in vivo and a useful element for enhancing the efficiency with which products coded by DNA vaccines are processed and presented in vivo. Because lemA(7–33) is particularly effective in protecting oligopeptides from proteases, this invention may have particular usefulness in enhancing local T cell at sites such as mucosal surfaces where there may be high proteolytic activity.

For more specific information about the invention or to request a copy of the patent application, please contact Peter Soukas at the telephone number or e-mail listed above. Additionally, please see a related article published in the Journal of Immunology at: 1999;163:6741–6747.

Dated: May 25, 2001.

Jack Spiegel,

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

[FR Doc. 01–13888 Filed 6–1–01; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Prospective Grant of Exclusive License: Development of Live, Attenuated Vaccines for Human Use Against Respiratory Syncytial Viruses Types A and B, and Parainfluenza Viruses Types 1, 2 and 3

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

ACTION: Notice.

SUMMARY: This is notice, in accordance with 35 U.S.C. 209(c)(1) and 37 CFR 404.7(a)(1)(i), that the National Institutes of Health (NIH), Department of Health and Human Services, is contemplating the grant of an exclusive license worldwide to practice the inventions embodied in the patent applications referenced below to American Home Products Corporation through its Wyeth-Ayerst Laboratories Division, Wyeth-Lederle Vaccines business unit, having a place of business in Madison, N.J. The United States of America is an assignee to the patent rights of these inventions.

USPA 09/291,894, filed 4/13/99, entitled ''Production of attenuated Chimeric RSV vaccines from cloned nucleotide sequences'' (now PCT/US00/08802, filed 3/31/00)

USPA 09/350,821, filed 7/9/99, entitled ''Recombinant PIV vaccines attenuated by deletion or ablation of non-essential gene'' (now PCT/US00/18523, filed 7/6/00)

USPA 60/143,132, filed 7/9/99, entitled ''Production of attenuated, human-bovine chimeric RSV vaccines'' (now USPA 09/602,212 and PCT/US00/17755, both filed 6/23/00)

USPA 60/143,425, filed 7/13/99, entitled ''Production of recombinant RSV expressing immune modulatory molecules'' (now USPA 09/614,285 and PCT/US00/19042, both filed 7/12/00)

USPA 60/143,097, filed 7/7/99, entitled ''Production of attenuated RSV vaccines involving modification of M2 open reading frame (ORF) 2'' (now USPA 09/611,829 and PCT/US00/18534, both filed 7/7/00)