

notice, especially regarding the estimated public burden and associated response time, should be directed to the: Office of Management And Budget, Office of Regulatory Affairs, New Executive Office Building, Room 10235, Washington, DC 20503, Attention: Desk Officer for NIH. To request more information on the proposed project or to obtain a copy of the data collection plans and instruments, contact: Dr. Debra Silverman, NCI Project Director, National Cancer Institute, Executive Plaza South, Room 8108, Rockville, Maryland 20892-7240, or call non-toll-free number (301) 435-4716, or FAX your request to (301) 402-1819, or E-mail your request, including your address, to Silvermd@exchange.nih.gov.

#### Comments Due Date

Comments regarding this information collection are best assured of having their full effect if received on or before January 11, 2001.

Dated: December 1, 2000.

**Reesa Nichols,**

*OMB Project Clearance Liaison.*

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## 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](mailto:soukasp@od.nih.gov). A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

#### Antibodies and Other Ligands Directed Against KIR2DL4 Receptor for Production of Interferon-Gamma

Eric Long, Sumati Rajagopalan (NIAID)  
DHHS Reference No. E-255-00/0 filed  
23 Oct 2000

Interferon-gamma is a potent antiviral and antimicrobial substance produced by natural killer (NK) white blood cells. NK cells are activated during infections by viruses and by other intracellular pathogens, such as parasites and bacteria. Soluble substances, such as interleukins, produced by infected cells activate NK cells to secrete interferon-gamma. Injection of interleukins into patients to stimulate NK cells to secrete interferon-gamma has not been a successful therapeutic approach because of the toxicity involved. The invention is based on the discovery by the inventors that activation of the KIR2DL4 receptor expressed by all NK cells stimulates them to produce interferon-gamma. The invention claims monoclonal antibodies and derivatives thereof, as well as natural and synthetic ligands of KIR2DL4 that can be utilized to stimulate interferon-gamma production by NK cells without any other stimulus. The possibility of inducing interferon-gamma production by NK cells without the toxic side effects of interleukins could be an effective therapy for various types of infections and of cancers. Also claimed in the invention are methods of treating various cancers and viral infections, methods of treating autoimmune disease, and methods of administration of the antibody or derivatives thereof.

#### Ixodes scapularis Tissue Factor Pathway Inhibitor

Ivo Francischetti, Jesus Valenzuela, Jose Ribeiro (NIAID)  
DHHS Reference No. E-208-00/0 filed  
05 Oct 2000

*Ixodes scapularis* is a blood-sucking tick and the principal vector of Lyme disease, a spirochetal illness caused by *Borrelia burgdorferi* and now the most common vector-borne infection in the United States; more than 50,000 cases have been reported during the last ten years. The salivary gland of *I. scapularis* has a number of pharmacologically active molecules that help the tick to successfully feed on blood, such as inhibitors of complement system, in addition to coagulation and platelet aggregation inhibitors. This invention describes Ixolaris, a protein that inhibits the initiation of blood coagulation by inhibition of components of the extrinsic pathway. Accordingly, Ixolaris blocks Factor X activation by Factor VIIa/TissueFactor, it attenuates Factor

Xa production by the prothrombinase, and inhibits fibrin formation in a diluted prothrombin time. Ixolaris is highly specific since it does not inhibit other serine proteases. Because Ixolaris has anticoagulant properties, it could be used to ameliorate a number of clinical conditions such as disseminated intravascular coagulation, and hypercoagulation states. In addition, Ixolaris may be useful as a vaccine candidate for Lyme disease because inactivation of Ixolaris by antibodies may make transmission of *Borrelia burgdorferi* more difficult. In addition to the composition of Ixolaris, the invention claims vaccines utilizing Ixolaris, methods of stimulating an immune response, and methods of treatment of restenosis, arterial thrombosis, and stroke.

#### Ixodes Salivary Anticomplement Protein

Jose Ribeiro (NIAID), Jesus Valenzuela (NIAID), Rosane Charlab (NIAID), Thomas Mather (EM)  
DHHS Reference No. E-207-00/0 filed  
28 Sep 2000

This invention describes Isac, a novel anticomplement protein that can be isolated and purified from *I. scapularis* (tick) saliva that may be useful as a peptide vaccine against Lyme disease. Because inactivation of Isac by antibodies will make transmission of *Borrelia burgdorferi* to humans more difficult, Isac is an ideal candidate for a Lyme disease vaccine. Isac disrupts the alternative complement pathway by inhibiting factors Bb and/or C3b, preventing cell lysis and anaphylatoxin production. The inventors have found no similarity to any protein in GenBank for Isac. Isac may also be used in situations where alternative complement activation is implicated such as in rheumatoid conditions such as lupus erythematosus or juvenile arthritis. The invention is further described in Ribeiro et al., "Purification, cloning, and expression of a novel salivary anticomplement protein from the tick, *Ixodes scapularis*," *J Biol. Chem.* 2000 Jun 23; 275(25):18717-23.

#### 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)  
DHHS Reference No. E-285-00/0 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 (FPLR1) as a receptor to chemoattract human peripheral blood neutrophils, monocytes, and T cells," *J Exp. Med.* 2000 Oct 2;192(7):1069-74.

#### **A Method for Bioconjugation Using Diels-Alder Cycloaddition**

Vince Pozsgay (NICHD)

DHHS Reference No. E-126-00/0 filed 09 Aug 2000

This invention relates to a new method for the synthesis of conjugate vaccines using the Diels-Alder cycloaddition reaction to covalently attach a carbohydrate antigen from a pathogen to a protein carrier. The Diels-Alder reaction has not been extended to conjugation involving biopolymers or other types of polymeric materials. Advantages of this method are that cross-linking during conjugation is entirely avoided in addition to the mild chemical conditions under which this synthesis method proceeds. Diels-Alder reactions commonly take place in high-temperature environments; the method contemplated by this invention takes place at much lower temperatures. In addition to claiming methods of synthesis for conjugate vaccines using the Diels-Alder cycloaddition, the patent application claims vaccines produced utilizing the method, and methods of inducing antibodies which

react with the polysaccharides contemplated by the invention.

#### **5-Substituted Derivatives of Conformationally Locked Nucleoside Analogues**

Victor Marquez, Pamela Russ (NCI)  
DHHS Reference No. E-249-00/0 filed 26 Jul 2000

This invention relates to 5-substituted derivatives of conformationally locked nucleoside analogues and methods of using these derivatives as antiviral and anticancer agents. The compounds contemplated by the invention are nucleoside analogues where the 5-substituent is a halogen, alkyl, alkene, halovinyl or alkyne group, and the nucleotide base is cytosine or uracil. The analogues are particularly effective in treating viral infections, specifically infections of DNA viruses such as Herpes simplex virus (HSV), Varicella zoster virus (VSV), Epstein Barr virus (EBV), and Cytomegalovirus (CMV) as well as members of the Poxviridae family. The inventors have demonstrated in plaque reduction assays that 5-substituted uracils (bromo, iodo, and bromovinyl) attached to a bicyclo[3.1.0]hexane template are thirty times more potent than acyclovir against HSV-1 and HSV-2.

#### **Bacteriophage Having Multiple Host Range**

Carl Merrill (NIMH), Sankar Adhya (NCI), Dean Scholl (NIMH)  
DHHS Reference No. E-257-00/0 filed 25 Jul 2000

Recently, there has been a renewed interest in the use of phages to treat bacterial infections. The inventors have discovered FK1-5, a highly lytic, non-lysogenic, stable bacteriophage with the ability to kill bacteria rapidly, making it a good candidate for phage therapy. The designation FK1-5 denotes the phage's ability to infect *E. coli* strains that contain the K1 polysaccharide in their outer capsule as well as *E. coli* strains that contain the K5 polysaccharide in their outer capsule. Sequence analysis of the tail proteins of phage FK1-5 by the inventors has shown that they are arranged in a cassette structure, suggesting that the host range of phages can be broadened to other K antigens, and even possibly other species of bacteria by recombinant techniques. FK1-5 has a particular advantage because it recognizes and attaches to the structures that confer virulence to bacteria. The inventors' demonstration that a phage can contain multiple tail proteins that expand its host range is useful for generating phage with broad-spectrum antibacterial properties for the

treatment of infectious diseases. The inventors have completed *in vitro* studies on this phage. Furthermore, because of the possibility of engineering the expression of recombinant tail proteins, gene transfer to organisms that are not normally infected by phages is also contemplated by the invention.

Dated: December 4, 2000.

**Jack Spiegel,**

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

[FR Doc. 00-31525 Filed 12-11-00; 8:45 am]

**BILLING CODE 4140-01-P**

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#### **A Mouse Model of UV-Inducible Cutaneous Malignant Melanoma**

Glenn Merlino *et al.* (NCI)  
DHHS Reference No. E-281-00/0  
*Licensing Contact:* Elaine White; 301/496-7056 ext. 282; e-mail: gese@od.nih.gov

The current invention embodies a genetically engineered mouse harboring a hepatocyte growth factor/scatter factor transgene ("HGF/SF"). The Met signaling pathway, which has been implicated in the development of human melanoma, is chronically