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)

USPA 60/143,134, filed 7/9/99, entitled ''Attenuated human-bovine chimeric PIV vaccines'' (now USPA 09/586,479 and PCT/US00/17066, both filed 6/15/00)
USPA 60/129,006, filed 4/13/99, entitled ''Production of attenuated negative stranded RNA virus vaccines from cloned nucleotides'' (now PCT/US00/09695, filed 4/12/00)
USPA 60/170,195, filed 12/10/99, entitled ''Use of recombinant PIVs as vectors to protect against infectious Diseases caused by PIV and other human Pathogens'' (now USPA 09/733,692 and PCT/US00/33293, both filed 12/8/00)
USPA 60/213,708, filed 6/23/00, entitled ''RSV vaccines expressing protective antigens from promoter-proximal genes''
USPA 60/215,809, filed 7/5/00, entitled ''Attenuated human-bovine chimeric PIV vaccines''
USPA 60/007,083, filed 9/27/95, entitled ''Production of infectious Respiratory Syncytial Virus from cloned nucleotide sequences'' (now USPA 08/720,132 and PCT/US96/15524, both filed 9/27/96)

The contemplated exclusive license may be limited to the development of live, attenuated vaccines for human use against Respiratory Syncytial Viruses Types A and B, and Parainfluenza Viruses Types 1, 2 and 3.

DATES: Only written comments and/or applications for a license which are received by the NIH Office of Technology Transfer on or before August 3, 2001 will be considered.

ADDRESSES: Requests for a copy of the patent application, inquiries, comments and other materials relating to the contemplated license should be directed to Uri Reichman, Ph.D., Technology Licensing Specialist, Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, MD 20852–3804; Telephone: (301) 496–7056, ext. 240; Facsimile: (301) 402–0220; E-mail: reichmau@od.nih.gov. A signed Confidential Disclosure Agreement will be required to receive copies of the patent application.

SUPPLEMENTARY INFORMATION: The Patent Applications cover a wide range of methods to produce live attenuated vaccines for PIV and RSV. This includes, for example, deletion or ablation of non-essential genes (PIV, USPA 09/350,821), insertion of genes expressing immune modulatory molecules (RSV, USPA 60/143,425), modification of the second translational open reading frame of the M2 gene (RSV, USPA 60/143,097), and shifts in gene positions that modulate expression of selected genes (RSV, USPA 60/213,708). It also includes human-bovine chimeric constructs (PIV, USPA 60/215,809, USPA 60/143,134; RSV, USPA 60/143,132) or RSV–PIV chimeric constructs (USPA 60/170,195 for PIV1,2,3 and USPA 09/291,894 for RSVA/B). US Provisional Application 60/129,006 relates to a new attenuation strategy applicable for the development of RSV and PIV vaccine candidates. It generally describes the finding that attenuating mutations identified in certain negative stranded RNA viruses are transferable to other viruses of the Mononegavirale order. US Provisional Application 60/007,083 describes an expression system for recovery of RSV viruses from the corresponding cDNA sequences.

The prospective exclusive license will be royalty-bearing and will comply with the terms and conditions of 35 U.S.C. 209 and 37 CFR 404.7. The prospective exclusive license may be granted unless, within 60 days from the date of this published Notice, NIH receives written evidence and argument that establishes that the grant of the license would not be consistent with the requirements of 35 U.S.C. 209 and 37 CFR 404.7.

Properly filed competing applications for a license filed in response to this notice will be treated as objections to the contemplated license. Comments and objections submitted in response to this notice will not be made available for public inspection, and, to the extent permitted by law, will not be released under the Freedom of Information Act, 5 U.S.C. 552.

Dated: May 25, 2001.

Jack Spiegel,

Director, Division of Technology Development and Transfer, Office of Technology Transfer.

[FR Doc. 01–13887 Filed 6–1–01; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF THE INTERIOR

Fish and Wildlife Service

Meeting of the Alaska Migratory Bird Co-management Council

AGENCY: Fish and Wildlife Service, Interior.

ACTION: Notice of meeting.

SUMMARY: The Alaska Migratory Bird Co-management Council has scheduled a public meeting to discuss financial needs and sources for funding the operation of the Council and the regional management bodies.

DATES: The Co-management Council will meet June 26, 2001.

ADDRESSES: The meeting will be conducted at the Hawthorn Suites Hotel at 1110 W. 8th Avenue in Anchorage, Alaska.

FOR FURTHER INFORMATION CONTACT: For additional information call Bob Stevens at 907/786–3499. Individuals with a disability who may need special accommodations in order to participate in the public comment portion of the meeting should call the above number.

SUPPLEMENTARY INFORMATION: The U.S. Fish and Wildlife Service formed the Alaska Migratory Bird Co-Management Council, which includes Native, State, and Federal representatives as equals, by means of a Notice of Decision published in the **Federal Register**, 65 FR 16405–16409, March 28, 2000. The amended Migratory Bird Treaty with Canada required the formation of such a management body. The Co-management Council will make recommendations for regulations for spring/summer subsistence harvesting of migratory birds in Alaska. In addition the Co-management Council will make recommendations regarding population and harvest monitoring, law enforcement policies, habitat protection, research and use of traditional knowledge, and education programs.

The meeting of the Co-management Council will begin at 8:30 a.m. on Tuesday, June 26, 2001. The session will end no later than 5 p.m. that day. The primary agenda item will be a discussion of funding alternatives for the operation of the Co-management Council and the regional management bodies that provide recommendations to the Co-management Council. The public is invited to attend. The Co-management Council will provide opportunities for public comment on agenda items at the end of the morning session and at the end of the afternoon session. Additional opportunities may be provided at the discretion of the Co-management Council. Agendas will be available at the door.

Dated: May 23, 2001.

David B. Allen,

Regional Director, Anchorage, Alaska.

[FR Doc. 01–13936 Filed 6–1–01; 8:45 am]

BILLING CODE 4310–55–P