



In which: X is either NH, O, or S; n is zero or a positive integer; R<sub>1</sub> is either CH<sub>2</sub>, NH, O, or S; R<sub>2</sub> is either CHR<sub>7</sub>, NR<sub>7</sub>, O, or S, in which R<sub>7</sub> is H or alkyl; R<sub>3</sub> and R<sub>4</sub>, which are either the same or different from each other, are either H, alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, alkyl-substituted aryl, (alkylsubstitutedaryl)alkyl, hydroxy-substituted alkyl, hydroxy-substituted aryl, or (hydroxy-substituted aryl)alkyl; R<sub>5</sub> is either CH<sub>2</sub>, NH, O, or S; and R<sub>6</sub> is either H or C(=Y)-R<sub>8</sub>-R<sub>9</sub>, in which: Y is either NH, O, or S; R<sub>8</sub> is either CHR<sub>10</sub>, NR<sub>10</sub>, O, or S, in which R<sub>10</sub> is H or alkyl; and R<sub>9</sub> is either H, alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, alkyl-substituted aryl, (alkyl-substituted aryl)alkyl, hydroxy-substituted alkyl, hydroxy-substituted aryl, or (hydroxy-substituted aryl)alkyl.

**Use of Protein Kinase C Delta Inhibitor, Specifically Rottlerin, Alone or in Further Combination With Staurosporine, in the Treatment of Metastatic Epithelioid Melanoma**

Denise Simmons (NCI), U.S. Provisional Application No. 60/531,876 filed 22 Dec 2003 (DHHS Reference No. E-311-2003/0-US-01).

Licensing Contact: Mojdeh Bahar; 301/435-2950; [baharm@mail.nih.gov](mailto:baharm@mail.nih.gov).

This invention is directed to the use of a protein kinase C delta inhibitor, specifically rottlerin, alone or in further combination with staurosporine, in the treatment of metastatic epithelioid melanoma. Preliminary studies show that treatment of cells from a metastasized human epithelioid melanoma with rottlerin reduced cellular proliferation by 90%, without

affecting proliferation or morphology of normal melanocytes. Cells from the matched primary site tumor of the same patient were not affected by this inhibitor, nor were cells from a matched tumor pair of fibroblastoid morphology obtained from a second patient. Treatment of cells from a metastasized human epithelioid melanoma with staurosporine caused an increase in branching and in the number of processes in the melanoma cells, without affecting cell number. These staurosporine-induced changes may be indicative of differentiation.

Dated: August 27, 2004.

**Steven M. Ferguson,**

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

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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, HHS.

**ACTION:** Notice.

**SUMMARY:** The inventions listed below are owned by an agency 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 Susan Ano, Ph.D., Technology Licensing Specialist, Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804; telephone: 301/435-5515; fax: 301/402-0220; e-mail: [anos@mail.nih.gov](mailto:anos@mail.nih.gov). A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

**Safer Attenuated Virus Vaccines With Missing or Diminished Latency of Infection**

*Jeffrey Cohen et al. (NIAID)*

U.S. Provisional Application Filed 28 Jun 2004 (DHHS Reference No. E-217-2004/0-US-01)

This technology describes recombinant viruses that have weakened ability to establish and/or maintain latency and their use as live vaccines. The viruses have one or more genetic mutations that allow for continued replication but that inhibit latency. The vaccine materials and methods for their construction are exemplified with the virus that causes chickenpox and whose latent infection results in shingles, a condition that affects up to an estimated 1 million people per year in the United States alone. Additionally, there are veterinary

applications of this technology. Specific examples of gene deletions, modifications, and/or insertions are described. Furthermore, replacement of these deleted genes with other desirable viral antigen encoding sequence(s) and/or cytokine genes in order to enhance a desired immunological response is also described. Aspects of this technology are relevant to other live virus vaccines, thus increasing the safety of such vaccines.

#### Anti-Vaccinia Monoclonal Antibody

Jonathan Yewdell et al. (NIAID)

DHHS Reference No. E-123-2004/0—  
Research Tool

The current technology describes a monoclonal antibody that reacts with a vaccinia virus protein abundantly expressed under an early viral promoter after infection of cells. The antibody is useful for quantitating vaccinia virus infected cells and for studying the function of the protein to which it binds, which is known to be a double stranded RNA binding protein involved in resistance of the virus to interferons. This antibody is available for licensing through a biological materials license agreement.

#### New Surrogate Marker for Diagnosis of HIV/AIDS Infection and for Evaluation of Treatment Effectiveness

Gene M. Shearer et al. (NCI)

U.S. Provisional Application 60/564,588  
Filed 23 Apr 2004 (DHHS Reference No.  
E-045-2004/0-US-01)

This technology describes the identification of a new surrogate marker, TNF-related apoptosis-inducing ligand (TRAIL), that can be universally employed to monitor the progression of HIV infection and other conditions and diseases associated with immune system activation and immunoassays for assessing the amount of TRAIL in a biological sample. In the case of HIV infection, measuring levels of this surrogate marker can distinguish among infected individuals with high viral load, infected individuals with low viral load, and uninfected individuals. Only two surrogate markers are currently recognized by the Food and Drug Administration as clinically relevant to HIV progression, HIV viral load and the absolute number of peripheral CD4 +T cells. Tests for assessing HIV viral load employ PCR, the use of which has drawbacks, including cross-contamination. TRAIL has mechanistic implications for HIV-1 pathogenesis and directly correlates to viral load but not necessarily inversely with CD4+ T cell count. Other surrogate markers have

been proposed but do not consistently reflect AIDS progression in all individuals or may result in overlooking possible treatments that may affect disease progression but do not affect the chosen marker. Therefore, use of this new surrogate marker to assess disease progression in infected individuals and to evaluate the effectiveness of various treatment regimens has several advantages over currently used methods.

#### Peptide Mimotopes of Lipooligosaccharide From Nontypeable *Haemophilus influenzae* and *Moraxella catarrhalis* as Peptide Vaccines

Xin-Xing Gu (NIDCD)

U.S. Provisional Application No. 60/  
441,928 Filed 22 Jan 2003 (DHHS  
Reference No. E-344-2002/0-US-01)

PCT Application No. PCT/US04/01457  
Filed 21 Jan 2004 (DHHS Reference No.  
E-344-2002/0-PCT-02)

U.S. Provisional Application No. 60/  
531,239 Filed 19 Dec 2003 (DHHS  
Reference No. E-083-2004/0-US-01)

U.S. Provisional Application No. 60/  
571,889 filed 17 May 2004 (DHHS  
Reference No. E-083-2004/1-US-01)

These inventions relate to peptide mimotopes of lipooligosaccharides (LOS) from nontypeable *Haemophilus influenzae* (NTHi) and *Moraxella catarrhalis* that are suitable for developing novel vaccines against the respective pathogens, for which there are currently no licensed vaccines. The mimotopes not only immunologically mimic LOS from NTHi and *Moraxella catarrhalis* but will also bind to antibodies specific for the respective LOS. NTHi and *Moraxella catarrhalis* are common pathogens that cause otitis media in children and lower respiratory tract infections in adults. The effectiveness of a vaccine could be increased by substitution of a LOS epitope with a peptide mimic. Preliminary experiments have shown that some of the mimic peptides conjugated to a carrier were as effective as their respective LOS-based vaccine in stimulating a humoral immune response in rabbits. A single consensus amino acid sequence was identified for *Moraxella catarrhalis*, while four such sequences were identified for NTHi. Thus, the identified peptides are promising candidates for developing novel vaccines for NTHi or *Moraxella catarrhalis*.

Dated: August 27, 2004.

Steven M. Ferguson,

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

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#### Vectors for Wild-Type DDR1b or DDR1b Mutant, and Production of THP-1 Cell Line Expressing Two DDR1 Isoforms, DDR1a and DDR1b

Teizo Yoshimura (NCI)

DHHS Reference No.: E-243-2004/0—  
Research Material.

Licensing Contact: Jesse S. Kindra;  
(301) 435-5559; kindraj@mail.nih.gov.

This technology relates to cloning of cDNAs coding for human discoidin domain receptor (DDR1) cDNAs (clone 11A for DDR1a and Clone 11B for DDR1b) from a human lung cDNA library; a mammalian expression vector for wild-type DDR1b or DDR1b mutant, and a THP-1 cell line expressing two DDR1 isoforms, DDR1a and DDR1b. These materials are useful to study the role and signaling pathways of DDR1 and to identify agonists or antagonists of these receptors.