[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, 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. 209 and 37 CFR Part 404 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.

FOR FURTHER INFORMATION: 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.

SUPPLEMENTARY INFORMATION: Technology descriptions follow.

Live Attenuated Vaccine to Prevent Disease Caused by West Nile Virus

Description of Technology: West Nile virus (WNV) has recently emerged in the U.S. and is considered a significant emerging disease that has embedded itself over a considerable region of the U.S. WNV infections have been recorded in humans as well as in different animals. From 1999-2014, WNV killed 1,765 people in the U.S. and caused severe disease in more than 41,762 others. This project is part of NIAID's comprehensive emerging infectious disease program.

The methods and compositions of this invention provide a means for prevention of WNV infection by immunization with attenuated, immunogenic viral vaccines against WNV. The invention involves a chimeric virus form comprising parts of WNV and Dengue virus. Construction of the hybrids and their properties are described in detail in multiple publications. The WNV chimeric vaccine does not target the central nervous system, which would be the case in an infection with wild type WNV. Importantly, two successful Phase I clinical trials were recently carried out with the vaccine. The live attenuated WNV vaccine is safe, well-tolerated, and immunogenic in healthy adult volunteers. Furthermore, the vaccine virus may also be considered for use as a safe reagent handled at bio-safety level 2 facilities for WNV diagnosis and surveillance.

Potential Commercial Applications:

• Human West Nile vaccine

• Veterinary West Nile vaccine

• West Nile Virus diagnostics

• West Nile Virus therapeutics

Competitive Advantages:

• Low cost of manufacture

• Proven chimeric vaccine technology

• Phase I clinical data available

Development Stage:

• In vivo data available (animal)

• In vivo data available (human)

Inventors: Alexander G. Pletnev, Robert M. Chanock, Joseph R. Putnak, Brian R. Murphy, Joseph E. Blaney, Stephen S. Whitehead (all of NIAID)

Publications:

1. Pletnev AG, et al. West Nile virus/dengue type 4 virus chimeras that are reduced in neurovirulence and peripheral virulence without loss of immunogenicity or protective efficacy. Proc Natl Acad Sci U S A. 2002 Mar 5;99(5):3036-41. [PMID 11880643]

2. Pletnev AG, et al. Molecularly engineered live-attenuated chimeric West Nile/dengue virus vaccines protect rhesus monkeys from West Nile virus. Virology. 2003 Sep 15;314(1):190-5. [PMID 14517072]

3. Hanley KA, et al. Infectivity of West Nile/dengue chimeric viruses for West Nile and dengue mosquito vectors. Vector Borne Zoonotic Dis. 2005 Spring;5(1):1-10. [PMID 15815144]

4. Pletnev AG, et al. Chimeric West Nile/dengue virus vaccine candidate: preclinical evaluation in mice, geese and monkeys for safety and immunogenicity. Vaccine. 2006 Sep 29;24(40-41):6392-404. [PMID 16831498]

5. Durbin AP, et al. The live attenuated chimeric vaccine rWN/DEN4delta30 is well-tolerated and immunogenic in healthy flavivirus-naïve adult volunteers. Vaccine. 2013 Nov 19;31(48):5772-7. [PMID 23968769]

6. Maximova OA, et al. Assurance of neuroattenuation of a live vaccine against West Nile virus: a comprehensive study of neuropathogenesis after infection with chimeric WN/DEN4delta30 vaccine in comparison to two parental viruses and a surrogate flavivirus reference vaccine. Vaccine. 2014 May 30;32(26):3187-97. [PMID 24736001]

Intellectual Property: HHS Reference No. E-357-2001/1 -

• US Patent No. 8,778,671 issued 15 Jul 2014

• US Patent Application No. 14/305,572 filed 16 Jun 2014

• Various international patents/applications issued/pending

Licensing Contact: Peter Soukas; 301-435-4646; ps193c@nih.gov

Three-Dimensional Curved Catheter for Right Atrial Appendage Traversal

Description of Technology: Available for licensing and commercial development is a three-dimensionally configured curved catheter for safe traversal of the

right atrial appendage (RAA). The device is configured to optimize one-way access of the pericardial space through the right atrium and into the RAA reducing the risk of coronary lacerations. Specifically the curved catheter is best described in three segments: a proximal segment, a transitional segment and a distal segment; the transition segment having a clockwise spiral shaped curvature. When inserted into a patient, the proximal segment is positioned within the inferior vena cava, the transition segment extends across the caval-atrial junction and curves rightward, forward, and upward such that the catheter abuts a right lateral wall of the right atrium, and the distal segment curves leftward, forward, and upward from the transition segment through the right atrium such that the catheter abuts an anterior wall of the right atrium adjacent to the RAA. The catheter is configured to guide a coaxial puncturing device to through the superior left sulcal wall of the RAA.

Potential Commercial Applications:

• Left atrial appendage ligation

• Circumferential tricuspid annuloplasty

• Epicardial ablation

Competitive Advantages: Reduced risk of coronary or myocardial laceration

Development Stage:

• Early-stage

• Prototype

Inventors: Robert Lederman (NHLBI), Toby Rogers (NHLBI), Nasser Rafiee (Mehr Medical), Adam Greenbaum (Henry Ford Hospital), William O'Neill (Henry Ford Hospital)

Intellectual Property: HHS Reference No. E-078-2015 - US Provisional Patent Application 62/162,453 filed May 15, 2015

Related Technologies: HHS Reference No. E-027-2013; HHS Reference No. E-115-2013; HHS Reference No. E-018-2014; and HHS Reference Nos. E-068-2014/E-124-2014

Licensing Contact: Michael Shmilovich, Esq.; 301-435-5019; shmilovm@mail.nih.gov

Collaborative Research Opportunity: The National Heart, Lung and Blood Institute is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize devices for pericardial interventional procedures. For collaboration opportunities, please contact Peg Koelble at 301-594-4095 or koelblep@nhlbi.nih.gov.

Pseudomonas Exotoxin A with Modified Furin Cleavage Site

Description of Technology: Immunotoxins kill cancer cells while allowing healthy, essential cells to survive. As a result, patients receiving immunotoxins are less likely to experience the deleterious side-effects associated with non-specific therapies such as chemotherapy. In order to make an effective immunotoxin, three components are generally required: a targeting domain, a furin cleavage site (FCS), and a toxic payload molecule (such as *Pseudomonas* exotoxin A (PE)). The purpose of the FCS is to allow the toxin domain to be processed by the target cell so that it can exert its toxic effect. This technology concerns the engineering of FCS in order to improve the efficacy of specific immunotoxins having distinct targeting domains. Several novel FCS have been

generated which can be substituted for the native FCS in PE. By using specific FCS with different targeting moieties, it is possible to engineer an immunotoxin that is better suited to treating specific types of cancer.

Potential Commercial Applications:

• Essential for the payload component of immunotoxins

• Treatment of any disease associated with increased or preferential expression of a specific cell surface receptor

• Specific diseases include hematological cancers, lung cancer (including mesothelioma), ovarian cancer, breast cancer, and head and neck cancers

Competitive Advantages:

• Designing specific furin cleavage sites for particular immunotoxins can improve cleavage and enhance toxin efficacy, resulting in improved therapeutic effectiveness

• Targeted therapy decreases non-specific killing of healthy, essential cells, resulting in fewer non-specific side-effects and healthier patients

Development Stage: In vitro data available

Inventors: Ira Pastan et al. (NCI)

Publications:

1. Weldon JE, et al. Designing the furin-cleavable linker in recombinant immunotoxins based on Pseudomonas exotoxin A. Bioconjug Chem. 2015 Jun 17;26(6):1120-8. [PMID 25997032]

2. Weldon JE, et al. A protease-resistant immunotoxin against CD22 with greatly increased activity against CLL and diminished animal toxicity" Blood. 2009 Apr 16;113(16):3792-800. [PMID 18988862]

Intellectual Property: HHS Reference No. E-197-2015/0-US-01 - US Provisional Application No. 62/163,667 filed May 19, 2015

Related Technologies:

• HHS Reference E-262-2005/0

• HHS Reference E-292-2007/0

• HHS Reference E-269-2009/0

• HHS Reference E-174-2011/0

• HHS Reference E-263-2011/0

Licensing Contact: David A. Lambertson, Ph.D.; 301-435-4632; lambertsond@mail.nih.gov

Collaborative Research Opportunity: The National Cancer Institute is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize Pseudomonas Exotoxin A with Modified Furin Cleavage Site. For collaboration opportunities, please contact John D. Hewes, Ph.D. at hewesj@mail.nih.gov.

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Richard U. Rodriguez, M.B.A.
Acting Director
Office of Technology Transfer
National Institutes of Health

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