

minimize suffering and death from influenza. Currently, there is not an effective way to vaccinate against avian influenza without knowing what subtype and strain will circulate. Described here are two technologies with application to development of vaccines against influenza as well as therapeutics and monoclonal antibodies. One technology provides for development of potentially broadly protective influenza vaccines, while the other seeks to improve immune response to the vaccine through increased receptor affinity.

The first technology offers candidate DNA vaccines that were primarily designed to elicit neutralizing antibodies to target H5N1, H1N1, H3N2 and other subtypes of influenza. The candidate vaccines express H/HA or neuramidase (N/NA) protein that has been codon optimized and/or modified at the protease cleavage site. The modified genes could be used in DNA vaccines, in viral vectors, recombinant proteins/particles or combination. Exemplary animal studies use proprietary expression systems that increase protein expression relative to commonly used alternatives. This invention potentially provides a vaccine strategy for controlling influenza epidemics, including avian flu, should it cross over to humans; the 1918 strain of flu; and seasonal flu strains. In addition, this invention is designed to lead to a combination vaccine to provide a broadly protective vaccine.

The second technology relates to H5N1 influenza vaccine candidates in which mutations have been introduced to increase affinity of the hemagglutinin (H or HA) for the sialic acid receptor found in humans, which have a different sialic acid linkage than the corresponding avian receptor. These mutations could therefore result in a higher immune response in vaccines, producing a more robust response than other H5N1 vaccine candidates that retain their avian receptor preferences. These mutations also changed antibody-sensitivity of the vaccine candidates. The H5 modifications can be expressed from DNA or adenoviral vectors, or the proteins themselves can be administered. Additionally, these mutated HAs can be used to develop therapeutic monoclonal antibodies. The technology describes three (3) unique monoclonal antibodies that react with wild-type H5, wild-type H5 and mutant HA equivalently, and the mutant HA, respectively.

**Applications and Advantages:** Influenza vaccine for pandemic or epidemic application; Therapeutic antibodies; Potential for combination

vaccine for broad protection, removing need for seasonal strain monitoring; DNA vaccines are easy to produce and store; No risk of reversion to pathogenic strain as with live-attenuated virus vaccines.

**Development Status Highlights:** Phase I clinical trial active for DNA vaccine candidate encoding H5, Indonesian strain (VRC-AVIDNA-036-00VP); Animal (mouse) data available; Codon optimized for expression in human cells.

**Publications:**

1. Certain aspects of this technology were published in: WP Kong *et al.* Protective immunity to lethal challenge of the 1918 pandemic influenza virus by vaccination. Proc Natl Acad Sci USA. 2006 Oct 24;103(43):15987-15991.

2. GJ Nabel. Gene-based influenza vaccines: a look to the future. Presentation to World Health Organization (WHO), February 2007; available online at [http://www.who.int/vaccine\\_research/diseases/influenza/160207\\_Nabel.pdf](http://www.who.int/vaccine_research/diseases/influenza/160207_Nabel.pdf).

**Inventors:** Gary J. Nabel *et al.* (VRC/NIAD).

**Patent Status:**

PCT patent application, serial number PCT/US2007/004506 (publication number WO 2007/100584), filed 16 Feb 2007 with priority to 16 Feb 2006 (HHS Reference No. E-116-2006/1-PCT-01).

PCT patent application, serial number PCT/US2007/081002, filed 10 Oct 2007 with priority to 10 Oct 2006 (HHS Reference No. E-306-2006/4-PCT-01).

**Related Technology:** U.S. Patent No. 7,094,598 issued 22 Aug 2006 (HHS Reference No. E-241-2001/1-US-01) and associated foreign rights (proprietary expression system with CMV/R promoter).

**Licensing Status:** Available for non-exclusive or exclusive licensing.

**Licensing Contact:** Susan Ano, PhD; 301-435-5515; [anos@mail.nih.gov](mailto:anos@mail.nih.gov).

**Polypeptides for Eliciting Neutralizing Antibodies Against HIV**

**Description of Technology:** The technology describes conjugate polypeptide compositions that are designed to elicit antibody response against HIV. The peptides are conjugates of one gp41 capable of forming a stable coiled-coil structure and another gp41 capable of forming an alpha-helical structure. These structural elements of gp41 were identified as important for playing a role in HIV-1 cell entry. Compositions that elicit neutralizing antibodies against HIV have been elusive to date, but the subject technology may be important in realizing that goal.

**Applications:** HIV vaccines; Neutralizing antibodies against HIV.

**Development Status:** Animal (rabbit and/or guinea pig) data available.

**Inventors:** Carol Weiss (FDA).

**Patent Status:** U.S. Patent 7,311,916 issued 28 Dec 2007 (HHS Reference No. E-212-2001/0-US-11).

**Licensing Status:** Available for non-exclusive licensing.

**Licensing Contact:** Susan Ano, PhD; 301-435-5515; [anos@mail.nih.gov](mailto:anos@mail.nih.gov).

**Collaborative Research Opportunity:** The FDA/CBER Laboratory of Immunology is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology. Please contact Carol Weiss at [carol.weiss@fda.hhs.gov](mailto:carol.weiss@fda.hhs.gov) for more information.

Dated: April 21, 2008.

**David Sadowski,**

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

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**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**National Institutes of Health**

**Center for Scientific Review; Amended Notice of Meeting**

Notice is hereby given of a change in the meeting of the Neurobiology of Learning and Memory Study Section, June 5, 2008, 8 a.m. to June 6, 2008, 5 p.m., One Washington Circle Hotel, One Washington Circle, Washington, DC, 20037 which was published in the **Federal Register** on April 4, 2008, 73 FR 18539-18542.

The meeting will be held one day only June 6, 2008. The meeting time and location remain the same. The meeting is closed to the public.

Dated: April 21, 2008.

**Jennifer Spaeth,**

*Director, Office of Federal Advisory Committee Policy.*

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