Licensing Status: Available for licensing.
Licensing Contact: Peter A. Soukas, J.D.; 301/435–4646; soukas@mail.nih.gov.

Improved Bacterial Host for Production of Anthrax Toxin Proteins and Vaccines: Bacillus anthracis BH450

Description of Invention: Anthrax toxin has previously been made from various avirulent strains of Bacillus anthracis. The inventors have genetically engineered a new strain of B. anthracis with improved properties. The strain, designated BH450, is totally deficient in the ability to make spores and to produce a major extracellular protease designated Peptidase M4. The genetic lesions introduced are defined, true deletions, so there is no possibility of reversion. Inability to make spores assures that laboratories growing the strain will not become contaminated with the very stable anthrax spores. Inability to make peptidase M4 increases the stability of proteins such as anthrax toxin that are secreted to the culture medium.
Applications and Modality: B. anthracis vaccine/prophylactic and therapeutic studies.
Market: Research tool useful for biodefense/therapeutic studies.
Developmen Status: The technology is a research tool.
Inventors: Andrei Pomerantsev, Dana Hsu, Ramakrishnan Sitaraman, Craig Galloway, Violetta Kivovich, Stephen Leplla (NIAID).
Licensing Status: This technology is not patented. The strain will be transferred through a Biological Materials License.
Licensing Contact: Peter A. Soukas, J.D.; 301/435–4646; soukas@mail.nih.gov.

Collaborative Research Opportunity: The National Institute of Allergy and Infectious Diseases, Laboratory of Bacterial Diseases, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize Bacillus anthracis BH450 strain. Please contact Dr. Andrei P. Pomerantsev at phone 301/451–9817 and/or e-mail apomerantsev@niaid.nih.gov for more information.

Monoclonal Antibodies That Neutralize B. anthracis Protective Antigen (PA), Lethal Factor (LF) and Edema Factor (EF)

Description of Invention: Anthrax, whether resulting from natural or bioterrorist-associated exposure, is a constant threat to human health. The lethality of anthrax is primarily the result of the effects of anthrax toxin, which has 3 components: a receptor-binding protein known as “protective antigen” (PA) and 2 catalytic proteins known as “lethal factor” (LF) and “edema factor” (EF). Although production of an efficient anthrax vaccine is an ultimate goal, the benefits of vaccination can be expected only if a large proportion of the population at risk is immunized. The low incidence of anthrax suggests that large-scale vaccination may not be the most efficient means of controlling this disease. In contrast, passive administration of neutralizing human or chimpanzee monoclonal antibody to a subject at risk for anthrax or exposed to anthrax could provide immediate efficacy for emergency prophylaxis against or treatment of anthrax.
Four monoclonal antibodies (mAbs) against PA, three mAbs against LF and four mAbs specific for EF of anthrax were isolated from a phage display library generated from immunized chimpanzees. Two mAbs recognizing PA (W1 and W2), two anti-LF mAbs efficiently neutralized the cytotoxicity of lethal toxin in a macrophage lysis assay. One anti-EF mAb efficiently neutralized edema toxin in cell culture. All five neutralizing mAbs protected animals from anthrax toxin challenge.
Application: Prophylactics or therapeutics against B. anthracis.
Developmental Status: Preclinical studies have been performed.
Inventors: Zhaochun Chen, Robert Purcell, Suzanne Emerson, Stephen Leplla, Mahtab Moyeri (NIAID).
Licensing Status: Available for exclusive or non-exclusive licensing.

Licensing Contact: Peter A. Soukas, J.D.; 301/435–4646; soukas@mail.nih.gov.
Collaborative Research Opportunity: The National Institute of Allergy and Infectious Diseases, Laboratory of Infectious Diseases is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize Chimpanzee/human neutralizing monoclonal antibodies against anthrax toxins. Please contact Dr. Robert Purcell at 301/496–5090 for more information.

Dated: September 18, 2008.
Richard U. Rodriguez,
Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.

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 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.

Inhibitors of the Plasmodial Surface Anion Channel as Antimalarials

Description of Technology: The inventions described herein are antimalarial small molecule inhibitors of the plasmodial surface anion channel (PSAC), an essential nutrient acquisition ion channel expressed on human
erythrocytes infected with malaria parasites. These inhibitors were discovered by high-throughput screening of chemical libraries and analysis of their ability to kill malaria parasites in culture. Two separate classes of inhibitors were found to work synergistically in combination against PSAC and killed malaria cultures at markedly lower concentrations than separately. These inhibitors have high affinity and specificity for PSAC and have acceptable cytotoxicity profiles. Preliminary in vivo testing of these compounds in a mouse malaria model is currently ongoing.

**Applications:** Treatment of malarial infections.

**Advantages:** Novel drug treatment for malarial infections; Synergistic effect of these compounds on PSAC.

**Development Status:** In vitro and in vivo data can be provided upon request.

**Market:** Treatment of malarial infection.

**Inventor:** Sanjay A. Desai (NIAID).

**Publications:**


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

**Licensing Contact:** Kevin W. Chang, PhD; 301–435–5018; changke@mail.nih.gov.

**Collaborative Research Opportunity:**
The NIAID Office of Technology Development is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize antimalarial drugs that target PSAC or other parasite-specific transporters. Please contact either Charles Rainwater or Dana Hsu at 301–496–2644 for more information.

**Aerosolized Vaccines**

**Description of Technology:** Vaccine delivery to humans by mucosal routes may offer some operational and immunological advantages over intramuscular administration by needle-and-syringe. Potential targets include the oral, nasal, rectal conjunctival, and vaginal surfaces with the oral and nasal routes being the most practical to consider for infants, children and adults of both sexes. Needle-free delivery methods may improve compliance, reduce discomfort, and improve safety of vaccines; particularly in the developing world, needle-free delivery could mitigate the risk of blood-borne pathogen transmission by unsafe injection practices or inadequately sterilized equipment, and be easier and safer to deploy by non-medical personnel.

**Applications:** Improved immunogenic compositions and vaccine formulations, delivery of viral vectors, plasmid DNA, proteins, and adjuvants.

**Development Status:** Vaccines have been formulated and preclinical studies have been performed.

**Inventors:** Mario Roederer and Srinivas Rao (NIAID).


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

**Licensing Contact:** Peter A. Soukas, J.D.; 301–435–4646; soukas@mail.nih.gov.

**Use of Saccharides Cross-Reactive With Bacillus anthracis Spore Glycoprotein as a Vaccine Against Anthrax**

**Description of Technology:** Bacillus anthracis is a spore-forming bacterium that causes anthrax in humans and in other mammals. The glycoprotein BclA (Bacillus collagen-like protein of anthracis) is a major constituent of the exosporium, the outermost surface of B. anthracis spores. The glycosyl part of BclA is an oligosaccharide composed of 2-O-methyl-4-(3-hydroxy-3-methylbutanamido)-4,6-dideoxy-d-glucose, referred to as anthrose, and three rhhamnose residues. A structure similar to anthrose, 4-(3-hydroxy-3-methylbutanamido)-4,6-dideoxy-d-glucose is found in the side chain of the capsular polysaccharide (CPS) of Shewanella spp. MR–4. Under certain growth conditions the bacteria produce a variant CPS lacking one methyl group on the hydroxybutyrate, 4-(3-hydroxybutanamido)-4,6-dideoxy-d-glucose. Contrary to anthrose, neither of the Shewanella CPSs is O-methylated.

The inventors have found that both Shewanella CPS variants react with anti-B. anthracis spore sera. The inventors have also found that these antisera reacted with flagellae of Pseudomonas syringae, reported to be glycosylated with a similar terminal saccharide, 4-(3-hydroxybutanamido)-4,6-dideoxy-2-O-methyl-d-glucose. Sera produced by immunization with Shewanella or P. syringae cells bound to B. anthracis spores but not to Bacillus cereus spores in a fluorescent microscopy assay. The inventors’ experiments show that methylation of the anthrose at the O–2 of the sugar ring and at the C–3 of 3-hydroxybutyrate are not essential for induction of cross-reactive antibodies.
The application claims the use of *Shewanella* CPS conjugates as a component of an anthrax vaccine. The application also claims the use of capsular polysaccharides from *Shewanella* and compounds from the flagella of *Pseudomonas syringae* for the development of anthrax vaccines.

**Application:** Development of anthrax vaccines, diagnostics and therapeutics.

**Development Status:** Conjugates have been synthesized and preclinical studies have been performed.

**Inventors:** Joanna Kubler-Kielb (NICHD), Rachel Schneerson (NICHD), Haijing Hu (NIAID), Stephen H. Leppla (NICHD), John B. Robbins (NICHD), Rachel Schneerson (NICHD), et al.

**Publication:** Kubler-Kielb. J. et al. Saccharides cross-reactive with *Bacillus anthracis* spore glycoprotein as an anthrax vaccine component. Proc Natl Acad Sci USA. 2008 Jun 24;105(25):8709–8712. This publication reports the preparation, characterization, and antibody responses to protein conjugates of the two variants of *Shewanella* CPS. Significantly, both conjugates induced antibodies that bound to both *Shewanella* CPS variants by ELISA and to *B. anthracis* spores, as detected by fluorescent microscopy.


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

**Licensing Contact:** Peter A. Soukas, J.D.; 301–435–4646; soukasp@mail.nih.gov.

### Modified Sugar Substrates and Methods of Use

**Description of Technology:** Glycans can be classified as linear or branched sugars. The linear sugars are the glycosaminoglycans comprising polymers of sulfated disaccharide repeat units that are O-linked to a core protein, forming a proteoglycan aggregate. The branched glycans are found as N-linked and O-linked sugars on glycoproteins or on glycolipids. These carbohydrate moieties of the linear and branched glycans are synthesized by a super family of enzymes, the glycosyltransferases (GTs), which transfer a sugar moiety from a sugar donor to an acceptor molecule. Although GTs catalyze chemically similar reactions in which a monosaccharide is transferred from an activated derivative, such as a UDP-sugar, to an acceptor, very few GTs bear similarity in primary structure.

Eukaryotic cells express several classes of oligosaccharides attached to proteins or lipids. Animal glycans can be N-linked via beta-GlcNAc to Asparagine (N-glycans), O-linked via UDP-GalNAc to Serine/Threonine (O-glycans), or can connect the carboxyl end of a protein to a phosphatidylinositol unit (GPI-anchors) via a common core glycan structure. Thus, there is potential to develop carbohydrate substrates comprising bioactive agents that can be used to produce glycoconjugates carrying sugar moieties with bioactive agents. Such glycoconjugates have many therapeutic and diagnostic uses, e.g. in labeling or targeted delivery. Further, such glycoconjugates can be used in the assembly of bio-nanoparticles to develop targeted-drug delivery systems or contrast agents for medical uses.

This application claims methods and compositions for making and using functionalized sugars. Also claimed in the application are methods for forming a wide variety of products at a cell or in an *in vitro* environment. More specifically, the claimed compositions of the invention comprise a sugar nucleotide and one or more functional groups.

**Applications:** Production of therapeutic or diagnostic glycoconjugates, assembly of bio-nanoparticles, development of contrast agents.

**Development Status:** Enzymes have been synthesized and initial studies have been performed.

**Inventors:** Pradman K. Qasba and Maria R. Manzoni (NCI).

**Publications:**
3. Analysis of antibody repertoires in NS2 proteins of influenza virus that produce glycoconjugates carrying sugar moieties with bioactive agents that can be used to develop glycoconjugates carrying sugar moieties with bioactive agents.

**Advantages:**
- Peptides can be expressed in a number of different expression systems;
- Peptides were identified based on the specificity of antibodies derived from human and avian influenza virus infected individuals.

**Development Status:** *In vitro* data can be provided upon request.

**Market:**
- Preventative or treatment for influenza virus infection; and
- Diagnostic for influenza virus infection.

**Inventors:** Hana Golding and Surender Khurana (FDA).

**Publications:**
3. Analysis of antibody repertoires in H5N1 infected and vaccinated...
individuals using influenza whole genome phage display at
"Immunobiology and Pathogenesis of
Influenza Infection", Atlanta: June 1–3,
2008. (poster presentation).

Patent Status: International Patent
Application PCT/US2008/067001 filed
13 Jun 2008 (HHS Reference No. E–236–

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

Licensing Contact: Kevin W. Chang,
Ph.D.; 301–435–5018;
changke@mail.nih.gov

Related Publications:
1. R Atarashi et al. Simplified
ultrasensitive prion detection by
recombinant PrP conversion with
shaking. Nat Methods 2008
Mar;5(3):211–212.
2. R Atarashi et al. Ultrasensitive
detection of scrapie prion protein
using seeded conversion of recombinant

Patent Status:
• PCT Application No. PCT/US2008/
070656 filed 21 Jul 2008 (HHS

• U.S. Application No. 12/177,012
filed 21 Jul 2008 (HHS Reference No. E–

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

Licensing Contact: RC Tang, JD, LLM;
301–435–5031; rctang@mail.nih.gov

Collaborative Research Opportunity:
The NIAID Laboratory of Persistent
Viral Diseases, TSE/Prion Biochemistry
Section, is seeking statements of
capability or interest from parties
interested in collaborative research to
further develop, evaluate, or
commercialize this technology. Please contact
Rosemary Walsh at 301–451–3528 or
rcwalsh@niaid.nih.gov.

Dated: September 18, 2008.

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

DEPARTMENT OF HEALTH AND
HUMAN SERVICES

National Institutes of Health

National Institute of Diabetes and
Digestive and Kidney Diseases;
Amended Notice of Meeting

Notice is hereby given of a change in the
meeting of the National Institute of Diabetes and Kidney
Diseases Special Emphasis Panel,
October 17, 2008, 2:30 p.m. to 3:30 p.m.,
National Institutes of Health, Two
Democracy Plaza, 6707 Democracy
Boulevard, Bethesda, MD 20892 which was
published in the Federal Register
on September 11, 2008, 73 FR 0177.
This meeting will be held October 22,
2008 instead of October 17, 2008. The
meeting is closed to the public.

Dated: September 18, 2008.

Jennifer Spaeth,
Director, Office of Federal Advisory
Committee Policy.

[FR Doc. E8–22604 Filed 9–25–08; 8:45 am]
BILLING CODE 4410–01–P

DEPARTMENT OF HEALTH AND
HUMAN SERVICES

National Institutes of Health

National Institute of Diabetes and
Digestive and Kidney Diseases; Notice of
Closed Meetings

Pursuant to section 10(d) of the
Federal Advisory Committee Act, as
amended (5 U.S.C. Appendix 2), notice is hereby given of the following
meetings.

The meetings will be closed to the public in accordance with the
provisions set forth in sections
552b(c)(4) and 552b(c)(6), Title 5 U.S.C.,
as amended. The grant applications and
the discussions could disclose
confidential trade secrets or commercial
property such as patentable material,
and personal information concerning
individuals associated with the grant
applications, the disclosure of which
would constitute a clearly unwarranted
invasion of personal privacy.

Name of Committee: National Institute of
Diabetes and Digestive and Kidney Diseases
Special Emphasis Panel, Molecular Therapy
Core Centers.

Date: October 21, 2008.

Time: 8 a.m. to 5 p.m.

Agenda: To review and evaluate grant
applications.

Place: Bethesda Marriott Suites, 6711
Democracy Boulevard, Bethesda, MD 20817.

Contact Person: Michele L. Barnard, PhD,
Scientific Review Officer, Review Branch,
DEA, NIDDK, National Institutes of Health,
Room 733, 6707 Democracy Boulevard,