In compliance with the requirements of Section 3506(c)(2)(A) of the Paperwork Reduction Act of 1995, the Administration for Children and Families is soliciting public comment on the specific aspects of the information collection described above. Copies of the proposed collection of information can be obtained and comments may be forwarded by writing to the Administration for Children and Families, Office of Planning, Research and Evaluation, 370 L'Enfant Promenade, SW., Washington, DC 20447, Attn: ACF Reports Clearance Officer. E-mail address: *OPREinfocollection@acf.hhs.gov.* All requests should be identified by the title of the information collection.

The Department specifically requests comments on (a) Whether the proposed collection of information is necessary for the proper performance of the functions of the agency, including whether the information will have practical utility; (b) the accuracy of the agency's estimate of the burden of the proposed collection of information; (c) the quality, utility, and clarity of the information to be collected; and (d) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques or other forms of information technology. Consideration will be given to comments and suggestions submitted within 60 days of this publication.

Dated: June 11, 2008.

Brendan C. Kelly,

OPRE Reports Clearance Officer.

[FR Doc. E8–13658 Filed 6–17–08; 8:45 am]

BILLING CODE 4184–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Administration for Children and Families

Submission for OMB Review; Comment Request Title: Community Based Child Abuse Prevention Program (CBCAP).

OMB No.: 0970–0155.

Description: The Program Instruction, prepared in response to the enactment of the Community-Based Grants for the Prevention of Child Abuse and Neglect (administratively known as the Community Based Child Abuse Prevention Program, (CECAP), as set forth in Title II of Pub. L. 108 36, Child Abuse Prevention and Treatment Act Amendments of 2003, and in the process of reauthorization, provides direction to the States and Territories to accomplish the purposes of (1) supporting community-based efforts to develop, operate, expand, and where appropriate to network, initiatives aimed at the prevention of child abuse and neglect, and to support networks of coordinated resources and activities to better strengthen and support families to reduce the likelihood of child abuse and neglect, and; (2) fostering an understanding, appreciation, and knowledge of diverse populations in order to be effective in preventing and treating child abuse and neglect. This Program Instruction contains information collection requirements that are found in Pub. L. 108–36 at Sections 201; 202; 203; 205; 206; 207; and pursuant to receiving a grant award. The information submitted will be used by the agency to ensure compliance with the statute, complete the calculation of the grant award entitlement, and provide training and technical assistance to the grantee.

Respondents: State Governments.

ANNUAL BURDEN ESTIMATES

Instrument	Number of respondents	Number of responses per respondent	Average burden hours per response	Total burden hours
Application	52	1	40	2,080
Annual Report	52	1	24	1,248
Estimated Total Annual Burden Hours				3,328

Additional Information:

Copies of the proposed collection may be obtained by writing to the Administration for Children and Families, Office of Administration, Office of Information Services, 370 L'Enfant Promenade, SW., Washington, DC 20447, Attn: ACF Reports Clearance Officer. All requests should be identified by the title of the information collection. E-mail address: *infocollection@acf.hhs.gov.*

OMB Comment:

OMB is required to make a decision concerning the collection of information between 30 and 60 days after publication of this document in the **Federal Register**. Therefore, a comment is best assured of having its full effect if OMB receives it within 30 days of publication. Written comments and recommendations for the proposed information collection should be sent directly to the following:

Office of Management and Budget, Paperwork Reduction Project. Fax: 202–395–6974. Attn: Desk Officer for the Administration for Children and Families.

Dated: June 11, 2008.

Janean Chambers,

Reports Clearance Officer.

[FR Doc. E8–13661 Filed 6–17–08; 8:45 am]

BILLING CODE 4184–01–M

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 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.

Use of Amyloid Proteins as Vaccine Scaffolds

Description of Technology: Amyloid proteins are composed of peptides whose chemical properties are such that they spontaneously aggregate in vitro or in vivo, assuming parallel or antiparallel beta sheet configurations. Amyloid proteins can arise from peptides which, though differing in primary amino acid sequences, assume the same tertiary and quaternary structures. The amyloid structure presents a regular array of accessible N–termini of the peptide molecules.

Claimed in this application are compositions and methods for use of amyloid proteins as vaccine scaffolds, on which peptide determinants from microorganisms or tumors may be presented to more efficiently generate and produce a sustained neutralizing antibody response to prevent infectious diseases or treat tumors. The inventors have arrayed peptides to be optimally immunogenic on the amyloid protein scaffold by presenting antigen using three different approaches. First, the N-terminal ends of the amyloid forming peptides can be directly modified with the peptide antigen of interest; second, the N-termini of the amyloid forming peptides are modified with a linker to which the peptide antigens of interest are linked; and third, the scaffold amyloid may be modified to create a chimeric molecule.

Aside from stability and enhanced immunogenicity, the major advantages of this approach are the synthetic nature of the vaccine and its low cost. Thus, concerns regarding contamination of vaccines produced from cellular substrates, as are currently employed for some vaccines, are eliminated; the robust stability allows the amyloid based vaccine to be stored at room temperature for prolonged periods of time; and the inexpensive synthetic amino acid starting materials, and their rapid spontaneous aggregation in vitro should provide substantial cost savings over the resource and labor-intensive current vaccine production platforms.

Application: Immunization to prevent infectious diseases or treat chronic conditions or cancer.

Development Status: Vaccine candidates have been synthesized and preclinical studies have been performed.

Inventors: Amy Rosenberg (CDER/FDA), James E. Keller (CBER/FDA), Robert Tycko (NIDDK).

Patent Status: PCT Application No. PCT/US2008/059499 filed 04 Apr 2008, claiming priority to 06 Apr 2007 (HHS Reference No. E–106–2007/0–PCT–02).

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

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

Collaborative Research Opportunity: The FDA, Division of Therapeutic Proteins (CDER) and Office of Vaccines, Division of Bacterial Products (CBER) is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize amyloid based vaccines for prevention of infectious disease or treatment of malignant states. Please contact Amy Rosenberg at *amy.rosenberg@fda.hhs.gov* or (301) 827–1794 for more information.

Immunostimulatory Combinations of TLR Ligands and Methods of Use

Description of Technology: New drugs or therapies that act by stimulating the immune system, or alternatively inhibiting certain aspects of the immune system, may be useful for treating various diseases or disorders, for example viral diseases, neoplasias, and/or allergies, and may also have use as vaccine adjuvants. However, although adjuvants have been suggested for use in vaccine compositions, there is an unmet need for adjuvants that can effectively enhance immune response.

Development of innate and adaptive immunity critically depends on the engagement of pattern recognition receptors (PRRs), which specifically detect microbial components named pathogen-or microbe-associated molecular patterns (PAMPs or MAMPs) (1–4). Toll-like receptors (TLRs) represent an important group of PRRs that can sense PAMPs or MAMPs once in the body. TLRs are widely expressed by many types of cells, for example cells in the blood, spleen, lung, muscle and intestines.

The present invention claims immunostimulatory combinations of TLR ligands and therapeutic and/or prophylactic methods that include administering an immunostimulatory combination to a subject. In general, the immunostimulatory combinations can provide an increased immune response compared to other immunostimulatory combinations and/or compositions. More specifically, combinations of TLR 2, 3 and 9 are claimed. The application also describes a novel mechanism for TLR synergy in terms of both signaling pathways and cytokine combinations.

Application: Development of improved adjuvants and/or synergistic combinations of adjuvants for vaccines.

Development Status: Compositions have been synthesized and preclinical studies have been performed.

Inventors: Jay Berzofsky and Qing Zhu (NCI).

Patent Status: U.S. Provisional Application No. 60/995,212 filed 24 Sep 2007 (HHS Reference No. E–298–2007/0–US–01).

Licensing Status: Available for exclusive or nonexclusive licensing.

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

Collaborative Research Opportunity: The National Cancer Institute's Vaccine Branch is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this invention of synergistic combinations of TLR ligands. Please contact John D. Hewes, PhD at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Catalytic Domains of [beta](1,4)-galactosyltransferase I Having Altered Donor and Acceptor Specificities, Domains That Promote In Vitro Protein Folding, and Methods for Their Use

Description of Technology: [beta](1,4)-galactosyltransferase I catalyzes the transfer of galactose from the donor, UDP-galactose, to an acceptor, N-acetylglucosamine, to form a galactose-[beta](1,4)-N-acetylglucosamine bond. This reaction allows galactose to be linked to an N-acetylglucosamine that may itself be linked to a variety of other molecules. The reaction can be used to make many types of molecules having great biological significance. For example, galactose-[beta](1,4)-N-acetylglucosamine linkages are very important for cellular recognition and binding events as well as cellular interactions with pathogens, such as viruses. Therefore, methods to synthesize these types of bonds have many applications in research and medicine to develop pharmaceutical agents and improved vaccines that can be used to treat disease.

The present invention is based on the surprising discovery that the enzymatic activity of [beta](1,4)-galactosyltransferase can be altered such that the enzyme can make chemical bonds that are very difficult to make by other methods. These alterations involve mutating the enzyme such that the mutated enzyme can transfer many different types of sugars from sugar nucleotide donors to many different types of acceptors. Therefore, the mutated [beta](1,4)-galactosyltransferases of the invention

can be used to synthesize a variety of products that, until now, have been very difficult and expensive to produce.

The invention also provides amino acid segments that promote the proper folding of a galactosyltransferase catalytic domain and mutations in the catalytic domain that enhance folding efficiency and make the enzyme stable at room temperature. The amino acid segments may be used to properly fold the galactosyltransferase catalytic domains of the invention and thereby increase their activity. The amino acid segments may also be used to increase the activity of galactosyltransferases that are produced recombinantly. Accordingly, use of the amino acid segments according to the invention allows for production of [beta](1,4)-galactosyltransferases having increased enzymatic activity relative to [beta](1,4)-galactosyltransferases produced in the absence of the amino acid segments.

Applications: Synthesis of polysaccharide antigens for conjugate vaccines, glycosylation of monoclonal antibodies, and as research tools.

Development Status: The enzymes have been synthesized and preclinical studies have been performed.

Inventors: Pradman K. Qasba, Boopathy Ramakrishnan, Elizabeth Boeggeman (NCI).

Patent Status: U.S. and Foreign Rights Available (HHS Reference No. E–230–2002/2).

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

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

Collaborative Research Opportunity: The National Cancer Institute's Nanobiology Program is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize the use of galactose and modified galactose to be linked to an N-acetylglucosamine that may itself be linked to a variety of other molecules. Please contact John D. Hewes, Ph.D. at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Methods of Glycosylation and Bioconjugation

Description of Technology: Eukaryotic cells express several classes of oligosaccharides attached to proteins or lipids. Animal glycans can be N-linked via beta-GlcNAc to Asn (N-glycans), O-linked via -GalNAc to Ser/Thr (O-glycans), or can connect the carboxyl end of a protein to a phosphatidylinositol unit (GPI-anchors) via a common core glycan structure. Beta (1,4)-galactosyltransferase I catalyzes the transfer of galactose from the donor, UDP-galactose, to an acceptor, N-acetylglucosamine, to form a galactose-beta (1,4)-N-acetylglucosamine bond, and allows galactose to be linked to an N-acetylglucosamine that may itself be linked to a variety of other molecules. Examples of these molecules include other sugars and proteins. The reaction can be used to make many types of molecules having great biological significance. For example, galactose-beta (1,4)-N-acetylglucosamine linkages are important for many recognition events that control how cells interact with each other in the body, and how cells interact with pathogens. In addition, numerous other linkages of this type are also very important for cellular recognition and binding events as well as cellular interactions with pathogens, such as viruses. Therefore, methods to synthesize these types of bonds have many applications in research and medicine to develop pharmaceutical agents and improved vaccines that can be used to treat disease.

The invention provides *in vitro* folding methods for a polypeptidyl-alpha-N-acetylgalactosaminyltransferase (pp-GalNAc-T) that transfers GalNAc to Ser/Thr residue on a protein. The application claims that this *in vitro*-folded recombinant ppGalNAc-T enzyme transfers modified sugar with a chemical handle to a specific site in the designed C-terminal polypeptide tag fused to a protein. The invention provides methods for engineering a glycoprotein from a biological substrate, and methods for glycosylating a biological substrate for use in glycoconjugation. Also included in the invention are diagnostic and therapeutic uses.

Application: Enzymes and methods are provided that can be used to promote the chemical linkage of biologically important molecules that have previously been difficult to link.

Development Status: Enzymes have been synthesized and characterization studies have been performed.

Inventors: Pradman Qasba and Boopathy Ramakrishnan (NCI).

Patent Status: U.S. Provisional Application No. 60/930,294 filed 14 May 2007 (HHS Reference No. E–204–2007/0–US–01).

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

Licensing Contact: Peter A. Soukas, J.D.; 301/435–4646; *soukasp@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 this technology. Please contact John D. Hewes, Ph.D. at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Alpha 1–3 N–Acetylgalactosaminyltransferases With Altered Donor and Acceptor Specificities, Compositions, and Methods of Use

Description of Technology: The present invention relates to the field of glycobiology, specifically to glycosyltransferases. The present invention provides structure-based design of novel glycosyltransferases and their biological applications.

The structural information of glycosyltransferases has revealed that the specificity of the sugar donor in these enzymes is determined by a few residues in the sugar-nucleotide binding pocket of the enzyme, which is conserved among the family members from different species. This conservation has made it possible to reengineer the existing glycosyltransferases with broader sugar donor specificities. Mutation of these residues generates novel glycosyltransferases that can transfer a sugar residue with a chemically reactive functional group to N–acetylglucosarnine (GlcNAc), galactose (Gal) and xylose residues of glycoproteins, glycolipids and proteoglycans (glycoconjugates). Thus, there is potential to develop mutant glycosyltransferases to produce glycoconjugates carrying sugar moieties with reactive groups that can be used in the assembly of bio-nanoparticles to develop targeted-drug delivery systems or contrast agents for medical uses.

Accordingly, methods to synthesize N–acetylglucosamine linkages have many applications in research and medicine, including in the development of pharmaceutical agents and improved vaccines that can be used to treat disease.

This application claims compositions and methods based on the structure-based design of alpha 1–3 N–Acetylgalactosaminyltransferase (alpha 3 GalNAc–T) mutants from alpha l–3galactosyltransferase (a3Gal–T) that can transfer 2′-modified galactose from the corresponding UDP-derivatives due to mutations that broaden the alpha 3Gal–T donor specificity and make the enzyme alpha3 GalNAc–T.

Application: Development of pharmaceutical agents and improved vaccines.

Development Status: Enzymes have been synthesized and preclinical studies have been performed.

Inventors: Pradman Qasba, Boopathy Ramakrishnan, Elizabeth Boeggman, Marta Pasek (NCI).

Patent Status: PCT Patent Application filed 22 Aug 2007 (HHS Reference No. E–279–2007/0–PCT–01).

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

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

Collaborative Research Opportunity: The National Cancer Institute's Nanobiology Program is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize structure-based design of novel glycosyltransferases. Please contact John D. Hewes, PhD at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Beta 1,4–Galactosyltransferases With Altered Donor and Acceptor Specificities, Compositions and Methods of Use

Description of Technology: The present invention relates to the field of glycobiology, specifically to glycosyltransferases. The present invention provides structure-based design of novel glycosyltransferases and their biological applications.

The structural information of glycosyltransferases has revealed that the specificity of the sugar donor in these enzymes is determined by a few residues in the sugar-nucleotide binding pocket of the enzyme, which is conserved among the family members from different species. This conservation has made it possible to reengineer the existing glycosyltransferases with broader sugar donor specificities. Mutation of these residues generates novel glycosyltransferases that can transfer a sugar residue with a chemically reactive functional group to N–acetylglucosarnine (GlcNAc), galactose (Gal) and xylose residues of glycoproteins, glycolipids and proteoglycans (glycoconjugates). Thus, there is potential to develop mutant glycosyltransferases to produce glycoconjugates carrying sugar moieties with reactive groups that can be used in the assembly of bio-nanoparticles to develop targeted-drug delivery systems or contrast agents for medical uses.

Accordingly, methods to synthesize N–acetylglucosamine linkages have many applications in research and medicine, including in the development of pharmaceutical agents and improved vaccines that can be used to treat disease.

The invention claims beta (1,4)–galactosyltransferase I mutants having altered donor and acceptor and metal ion specificities, and methods of use thereof. In addition, the invention claims methods for synthesizing oligosaccharides using the beta (1,4)–galactosyltransferase I mutants and to using the beta (1,4)–galactosyltransferase I mutants to conjugate agents, such as therapeutic agents or diagnostic agents, to acceptor molecules. More specifically, the invention claims a double mutant beta 1,4 galactosyltransferase, human beta–1,4–Tyr289Leu–Met344His–Gal–T1, constructed from the individual mutants, Tyr289Leu–Gal–T1 and Met344His–Gal–T1, that transfers modified galactose in the presence of magnesium ion, in contrast to the wild-type enzyme which requires manganese ion.

Application: Development of pharmaceutical agents and improved vaccines.

Development Status: Enzymes have been synthesized and preclinical studies have been performed.

Inventors: Pradman Qasba, Boopathy Ramakrishnan, Elizabeth Boeggman (NCI).

Patent Status: PCT Patent Application filed 22 Aug 2007 (HHS Reference No. E–280–2007/0–PCT–01).

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

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

Collaborative Research Opportunity: The National Cancer Institute's Nanobiology Program is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize glycosyltransferases. Please contact John D. Hewes, Ph.D., Technology Transfer Specialist, NCI, at (301) 435–3121 or *hewesj@nail.nih.gov.*

Bioreactor Device and Method and System for Fabricating Tissue

Description of Technology: Available for licensing and commercial development is a millifluidic bioreactor system for culturing, testing, and fabricating natural or engineered cells and tissues. The system consists of a millifluidic bioreactor device and methods for sample culture. Biologic samples that can be utilized include cells, scaffolds, tissue explants, and organoids. The system is microchip controlled and can be operated in closed-loop, providing controlled delivery of medium and biofactors in a sterile temperature regulated environment under tabletop or incubator use. Sample perfusion can be applied periodically or continuously, in a bidirectional or unidirectional manner, and medium re-circulated.

Advantages: The device is small in size, and of conventional culture plate format.

Provides the ability to grow larger biologic samples than microfluidic systems, while utilizing smaller medium volumes than conventional bioreactors. The bioreactor culture chamber is adapted to contain sample volumes on a milliliter scale (10 [mu]L to 1 mL, with a preferred size of 100 [mu]L), significantly larger than chamber volumes in microfluidic systems (on the order of 1 [mu]L). Typical microfluidic systems are designed to culture cells and not larger tissue samples.

The integrated medium reservoirs and bioreactor chamber design provide for, (1) Concentration of biofactors produced by the biologic sample, and (2) the use of smaller amounts of exogenous biofactor supplements in the culture medium. The local medium volume (within the vicinity of the sample) is less than twice the sample volume. The total medium volume utilized is small, preferably 2 ml, significantly smaller than conventional bioreactors (typically using 500–1000 mL).

Provides for real-time monitoring of sample growth and function in response to stimuli via an optical port and embedded sensors. The optical port provides for microscopy and spectroscopy measurements using transmitted, reflected, or emitted (e.g., fluorescent, chemiluminescent) light. The embedded sensors provide for measurement of culture fluid pressure and sample pH, oxygen tension, and temperature.

Capable of providing external stimulation to the biologic sample, including mechanical forces (e.g., fluid shear, hydrostatic pressure, matrix compression, microgravity via clinorotation), electrical fields (e.g., AC currents), and biofactors (e.g., growth factors, cytokines) while monitoring their effect in real-time via the embedded sensors, optical port, and medium sampling port.

Monitoring of biologic sample response to external stimulation can be performed non-invasively and non-destructively through the embedded sensors, optical port, and medium sampling port. Testing of tissue mechanical and electrical properties (e.g., stiffness, permeability, loss modulus via stress or creep test, electrical impedance) can be performed

over time without removing the sample from the bioreactor device.

The bioreactor sample chamber can be constructed with multiple levels fed via separate perfusion circuits, facilitating the growth and production of multiphasic tissues.

Application: Cartilage repair and methods for making tissue-engineered cartilage.

Development Status: Electrospinning method is fully developed and cartilage has been synthesized.

Inventors: Juan M. Taboas (NIAMS), Rocky S. Tuan (NIAMS), *et al.*

Patent Status: PCT Application No. PCT/US2006/028417 filed 20 Jul 2006, which published as WO 2007/012071 on 25 Jan 2007; claiming priority to 20 Jul 2005 (HHS Reference No. E–042–2005/0–PCT–02).

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

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

Cell-Nanofiber Composite Based Engineered Cartilage

Description of Technology: Available for licensing and commercial development is a tissue-engineered cartilage derived from a cellular composite made from a biodegradable, biocompatible polymeric nanofibrous matrix having dispersed chondrocytes or adult mesenchymal stem cells. More particularly, tissue-engineered cartilage can be prepared where the cartilage has a biodegradable and biocompatible nanofibrous polymer matrix prepared by electrospinning and a plurality of chondrocytes or mesenchymal stem cells dispersed in the pores of the matrix. The tissue-engineered cartilage possesses compressive strength properties similar to natural cartilage.

The electrospinning process is a simple, economical means to produce biomaterial matrices or scaffolds of ultra-fine fibers derived from a variety of biodegradable polymers (Li WJ, *et al., J. Biomed. Mater. Res.* 2002; 60:613–21). Nanofibrous scaffolds (NFSs) formed by electrospinning, by virtue of structural similarity to natural extracellular matrix (ECM), may represent promising structures for tissue engineering applications. Electrospun three-dimensional NFSs are characterized by high porosity with a wide distribution of pore diameter, high-surface area to volume ratio and morphological similarities to natural collagen fibrils (Li WJ, *et al., J. Biomed. Mater. Res.* 2002; 60:613–21). These physical characteristics promote favorable biological responses of seeded cells in vitro and in vivo, including enhanced cell attachment, proliferation, maintenance of the chondrocytic phenotype (Li WJ, et al., *J. Biomed. Mater. Res.* 2003; 67A: 1105–14), and support of chondrogenic differentiation (Li WJ, *et al., Biomaterials* 2005; 26:599–609) as well as other connective tissue lineage differentiation (Li WJ, *et al., Biomaterials* 2005; 26:5158–5166). The invention based on cell-nanofiber composite represents a candidate engineered tissue for cell-based approaches to cartilage repair.

Application: Cartilage repair and methods for making tissue-engineered cartilage.

Development Status: Electrospinning method is fully developed and cartilage has been synthesized.

Inventors: Wan-Ju Li and Rocky Tuan (NIAMS).

Publications: The invention is further described in:

1. W-J Li *et al.,* Engineering controllable anisotropy in electrospun biodegradable nanofibrous scaffolds for musculoskeletal tissue engineering. J Biomech. 2007; 40(8):1686–1693.

2. W-J Li *et al.,* Fabrication and characterization of six electrospun poly(alpha-hydroxy ester)-based fibrous scaffolds for tissue engineering applications. Acta Biomater. 2006 Jul; 2(4):377–385.

3. CK Kuo *et al.,* Cartilage tissue engineering: its potential and uses. Curr Opin Rheumatol. 2006 Jan; 18(1):64–73. Review.

4. W-J Li *et al.,* Multilineage differentiation of human mesenchymal stem cells in a three-dimensional nanofibrous scaffold. Biomaterials. 2005 Sep; 26(25):5158–5166.

Patent Status: PCT Application No. PCT/US2006/0237477 filed 15 Jun 2006, claiming priority to 15 Jun 2005 (HHS Reference No. E–116–2005/0–PCT–02).

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

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

Cell-Nanofiber Composite and Cell-Nanofiber Composite Amalgam Based Engineered Intervertebral Disc

Description of Technology: Diseased or damaged musculoskeletal tissues are often replaced by an artificial material, cadaver tissue or donated, allogenic tissue. Tissue engineering offers an attractive alternative whereby a live, natural tissue is generated from a construct made up of a patient's own cells or an acceptable/compatible cell source in combination with a biodegradable scaffold for replacement of defective tissue.

Degeneration of the intervertebral disc (IVD) is a common and significant source of morbidity in our society. Approximately 8 of 10 adults at some point in their life will experience an episode of significant low back pain, with the majority improving without any formal treatment. However, for the subject requiring surgical management current interventions focus on fusion of the involved IVD levels, which eliminates pain but does not attempt to restore disc function. Approximately 200,000 spinal fusions were performed in the United States in 2002 to treat pain associated with lumbar disc degeneration. Spinal fusion however is thought to significantly alter the biomechanics of the disc and lead to further degeneration, or adjacent segment disease. Therefore, in the past decade there has been mounting interest in the concept of IVD replacement. The replacement of the IVD holds tremendous potential as an alternative to spinal fusion for the treatment of degenerative disc disease by offering a safer alternative to current spinal fusion practices.

At the present time, several disc replacement implants are at different stages of preclinical and clinical testing. These disc replacement technologies are designed to address flexion, extension, and lateral bending motions; however, they do little to address compressive forces and their longevity is limited due to their inability to biointegrate. Therefore, a cell-based tissue engineering approach offers the most promising alternative to replace the degenerated IVD. Current treatment for injuries that penetrate subchondral bone include subchondral drilling, periosteal tissue grafting, osteochondral allografting, chondrogenic cell and transplantation; but are limited due to suboptimal integration with host tissues.

The present invention claims tissue engineered intervertebral discs comprising a nanofibrous polymer hydrogel amalgam having cells dispersed therein, methods of fabricating tissue engineered intervertebral discs by culturing a mixture of stem cells or intervertebral disc cells and a electrospun nanofibrous polymer hydrogel amalgam in a suitable bioreactor, and methods of treatment comprising implantation of tissue engineered intervertebral disc into a subject.

Application: Intervertebral disc bio-constructs and electrospinning methods for fabrication of the discs.

Development Status: Prototype devices have been fabricated and

preclinical studies have been performed.

Inventors: Wan-Ju Li, Leon Nesti, Rocky Tuan (NIAMS).

Patent Status: PCT Application No. PCT/US07/020974 filed 27 Sep 2007, claiming priority to 27 Sep 2006 (HHS Reference No. E–309–2006/2–PCT–01).

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

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

Methods for Preparing Bacillus anthracis Protective Antigen for Use in Vaccines

Description of Technology: This invention relates to improved methods of preparing *Bacillus anthracis* protective antigen (PA) from a cell or organism, particularly a recombinant cell or microorganism, for use in vaccines. Production and purification methods of modified PA from a non-sporogenic strain of *Bacillus anthracis* are described. Specifically, a scalable fermentation and purification process is claimed that is suitable for vaccine development, and that produces almost three times more product than earlier-reported processes. This is accomplished using a biologically inactive protease-resistant PA variant in a protease-deficient non-sporogenic avirulent strain of *B. anthracis* (BH445). One of the PA variants described in the patent application lacks the furin and chymotrypsin cleavage sites.

Advantages: Bacillus anthracis protective antigen is a major component of the currently licensed human vaccine (Anthrax Vaccine Adsorbed, AVA). Although the current human vaccine has been shown to be effective against cutaneous anthrax infection in animals and humans and against inhalation anthrax in rhesus monkeys, the licensed vaccine has several limitations: (1) AVA elicits a relatively high degree of local and systemic adverse reactions, probably mediated by variable amounts of undefined bacterial products, making standardization difficult; (2) the immunization schedule requires administration of six doses within an eighteen (18) month period, followed by annual boosters; (3) there is no defined vaccine-induced protective level of antibody to PA by which to evaluate new lots of vaccines; and (4) AVA is comprised of a wild-type PA. Thus a vaccine comprising a modified purified recombinant PA would be effective, safe, allow precise standardization, and require fewer injections.

The invention also relates to PA variants, and/or compositions thereof, which are useful for eliciting an immunogenic response in mammals, particularly humans, including responses that provide protection against, or reduce the severity of, infections caused by *B. anthracis.* The vaccines claimed in this application are intended for active immunization for prevention of *B. anthracis* infection, and for preparation of immune antibodies.

Application: Improved *B. anthracis* vaccines.

Development Status: Phase I clinical studies are being performed.

Inventors: Joseph Shiloach (NIDDK), Stephen Leppla (NIDCR), Delia Ramirez (NIDDK), Rachel Schneerson (NICHD), John Robbins (NICHD).

Publication: DM Ramirez *et. al.* Production, recovery and immunogenicity of the protective antigen from a recombinant strain of *Bacillus anthracis*. J Ind Microbiol Biotechnol. 2002 Apr;28(4):232–238.

Patent Status: U.S. Patent Application No. 10/290,712 filed 08 Nov 2002 (HHS Reference No. E–023–2002/0–US–02).

Licensing Status: Available for exclusive or nonexclusive licensing.

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

Collaborative Research Opportunity: The National Institutes of Health is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize methods of preparing *Bacillus anthracis* protective antigen (PA) from a cell or organism, particularly a recombinant cell or microorganism, for use in vaccines. Please contact Rochelle S. Blaustein, J.D., at 301/451–3636 or *Rochelle.Blaustein@nih.gov* for additional information.

Recombinant Modified Bacillus anthracis Protective Antigen for Use in Vaccines

Description of Technology: This invention relates to improved methods of preparing *Bacillus anthracis* protective antigen (PA) for use in vaccines. PA is a secreted, non-toxic protein with a molecular weight of 83 KDa. PA is a major component of the currently licensed human vaccine (Anthrax Vaccine Adsorbed, AVA). Although the licensed human vaccine has been shown to be effective against cutaneous anthrax infection in animals and humans and against inhalation anthrax in rhesus monkeys, the licensed vaccine has several limitations: (1) AVA elicits a relatively high degree of local and systemic adverse reactions, probably mediated by variable amounts of undefined bacterial products, making standardization difficult; (2) the immunization schedule requires administration of six doses within an eighteen (18) month period, followed by annual boosters; (3) there is no defined vaccine-induced protective level of antibody to PA by which to evaluate new lots of vaccines; and (4) AVA is comprised of a wild-type PA. It has been suggested that a vaccine comprising a modified purified recombinant PA would be effective, safe, allow precise standardization, and require fewer injections.

This invention claims methods of producing and recovering PA from a cell or organism, particularly a recombinant cell or microorganism. The invention claims production and purification of modified PA from a non-sporogenic strain of *Bacillus anthracis*. In contrast to other previously described methods, greater quantities of PA are obtainable from these cells or microorganisms. Specifically, a scalable fermentation and purification process is claimed that is suitable for vaccine development, and that produces almost three times more product than earlier-reported processes. This is accomplished using a biologically inactive protease-resistant PA variant in a protease-deficient non-sporogenic avirulent strain of *B. anthracis* (BH445). One of the PA variants described in the patent application lacks the furin and chymotrypsin cleavage sites.

The invention relates to improved methods of producing and recovering sporulation-deficient *B. anthracis* mutant strains, and for producing and recovering recombinant *B. anthracis* protective antigen (PA), especially modified PA which is protease resistant, and to methods of using of these PAs or nucleic acids encoding these PAs for eliciting an immunogenic response in humans, including responses which provide protection against, or reduce the severity of, *B. anthracis* bacterial infections and which are useful to prevent and/or treat illnesses caused by *B. anthracis*, such as inhalation anthrax, cutaneous anthrax and gastrointestinal anthrax.

Application: Improved *B. anthracis* vaccines.

Development Status: Phase I clinical studies are being performed.

Inventors: Stephen Leppla (NIDCR), M. J. Rosovitz (NIDCR), John Robbins (NICHD), Rachel Schneerson (NICHD).

Patent Status: U.S. Patent No. 7,261,900 issued 28 Aug 2007 (HHS Reference No. E–268–2002/0–US–02); U.S. Patent Application No. 11/831,860 filed 31 Jul 2007 (HHS Reference No. E–268–2002/0–US–03).

Licensing Status: Available for exclusive or nonexclusive licensing.

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

γPGA Conjugates for Eliciting Immune Responses Directed Against Bacillus anthracis and Other Bacilli

Description of Technology: This invention claims immunogenic conjugates of a poly-γ-glutamic acid (γPGA) of *B. anthracis*, or of another bacillus that expresses a γPGA that elicit a serum antibody response against *B. anthracis*, in mammalian hosts to which the conjugates are administered. The invention also relates methods which are useful for eliciting an immunogenic response in mammals, particularly humans, including responses which provide protection against, or reduce the severity of, infections caused by *B. anthracis*. The vaccines claimed in this application are intended for active immunization for prevention of *B. anthracis* infection, and for preparation of immune antibodies. The vaccines of this invention are designed to confer specific immunity against infection with *B. anthracis*, and to induce antibodies specific to *B. anthracis* γPGA. The *B. anthracis* vaccine is composed of non-toxic bacterial components, suitable for infants, children of all ages, and adults.

Inventors: Rachel Schneerson (NICHD), Stephen Leppla (NIAID), John Robbins (NICHD), Joseph Shiloach (NIDDK), Joanna Kubler-Kielb (NICHD), Darrell Liu (NIDCR), Fathy Majadly (NICHD).

Publication: R Schneerson *et al.* Poly(gamma-D-glutamic acid) protein conjugates induce IgG antibodies in mice to the capsule of *Bacillus anthracis:* a potential addition to the anthrax vaccine. Proc Natl Acad Sci USA. 2003 Jul 22;100(15):8945–8950.

Patent Status: U.S. Patent Application No. 10/559,825 filed 02 Dec 2005, claiming priority to 05 Jun 2003 (HHS Reference No. E–343–2002/0–US–04).

Licensing Status: Available for licensing.

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

Methods for Conjugation of Oligosaccharides or Polysaccharides to Protein Carriers Through Oxime Linkages Via 3-Deoxy-D-Manno-Octulsonic Acid

Description of Technology: This technology comprises new methods for the conjugation of O-specific polysaccharides/oligosaccharides (O-SP/OS) derived from bacterial lipooligosaccharides/lipopolysaccharides (LOS/LPS), after their cleavage from Lipid A, to carrier proteins, to serve as potential vaccines. Conjugation is performed between the carbonyl group on the terminal reducing end of the saccharide and the aminooxy group of a bifunctional linker bound further to the protein.

The inventors have carried out the reaction under mild conditions and in a short time resulting in binding 3-deoxy-D-manno-octulosonic acid (KDO) on the sacchride to the protein. These conjugates preserve the external non-reducing end of the sacchride, are recognized by antisera, and induce immune responses in mice to both conjugate components (*i.e.*, the OS and the associated carrier protein).

Application: Cost effective and efficient manufacturing of conjugate vaccines.

Inventors: Joanna Kubler-Kielb (NICHD), Vince Pozsgay (NICHD), Gil Ben-Menachem (NICHD), Rachel Schneerson (NICHD), *et al.*

Patent Status: PCT Application No. PCT/US2007/016373 filed 18 Jul 2007, which published as WO 2008/013735 on 31 Jan 2008; claiming priority to 21 Jul 2006 (HHS Reference No. E–183–2005/0–PCT–02).

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

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

Dated: June 10, 2008.

Richard U. Rodriguez,

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

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 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.

Construction of Recombinant Baculoviruses Carrying the Gene Encoding the Major Capsid Protein, VP1, From Calicivirus Strains (Including Norovirus Strains Toronto, Hawaii, Desert Shield, Snow Mountain, and MD145–12)

Description of Technology: The noroviruses (known as ''Norwalk-like viruses'') are associated with an estimated 23,000,000 cases of acute gastroenteritis in the United States each year. Norovirus illness often occurs in outbreaks, affecting large numbers of individuals, illustrated recently by well-publicized reports of gastroenteritis outbreaks on several recreational cruise ships and in settings such as hospitals and schools. Norovirus disease is clearly important in terms of medical costs and missed workdays, and accumulating data support its emerging recognition as important agents of diarrhea-related morbidity.

Because the noroviruses cannot be propagated by any means in the laboratory, an important strategy in their study is the development of molecular biology-based tools. This invention reports the development of recombinant baculoviruses carrying the capsid gene from several caliciviruses associated with human disease. Growth of these baculovirus recombinants in insect cells results in the expression of virus-like particles (VLPs) that are antigenically indistinguishable from the native calicivirus particle. These VLPs can be purified in large quantities for use as diagnostic reagents and potential vaccine candidates.

Inventors: Kim Y. Green, Judy F. Lew, Adriene D. King, Stanislav V. Sosnovtsev, Gael M. Belliot (NIAID).

Publication: An example of the application of these materials is further described in KY Green *et al.*, ''A predominant role for Norwalk-like viruses as agents of epidemic gastroenteritis in Maryland nursing homes for the elderly,'' J. Infect. Dis. 2002 Jan. 15;185(2):133–146.

Patent Status: HHS Reference No. E–198–2003/0—Research Material.

Licensing Status: The materials embodied in this invention are available