Silica-Coated Nanodiamonds for Imaging and the Delivery of Therapeutic Agents

Description of Technology: NIH investigators invented a robust and easily implemented method of synthesizing silica-coated nanodiamonds for imaging and therapeutic applications. A patent estate covering these methods is offered for licensing to commercial entities. The method generally includes coating nanodiamonds with a silica precursor, e.g., tetraethylorthosilicate (TEOS), inside liposomes. The liposomes are then removed to yield a final product that is stable, monodisperse, and easy to functionalize.

Potential Commercial Applications:
- Imaging
- Drug delivery

Competitive Advantages:
- Small size
- Physiologically inert carrier
- Monodisperse
- Stable in aqueous solution
- Readily functionalized

Development Stage: Prototype.

Inventors: Ambika Bumb (NHLBI), Susanta Kumar Sarkar (NHLBI), Keir Neuman (NHLBI), Martin Brechbiel (NCI).

Publications:

1. Yu SJ, et al. Bright fluorescent nanodiamonds: no photobleaching and low cytotoxicity. J Am Chem Soc. 2005 Dec 21;127(50):17604–5. [PMID 16351080]
2. Wilson RM. Nanodiamonds are promising quantum probes of living cells. Phys Today 2011 Aug;64(8):17. [doi 10.1063/PT.3.1204]
3. Chow EK, et al. Nanodiamond therapeutic delivery agents mediate enhanced chemoresistant tumor treatment. Sci Transl Med. 2011 Mar 9;3(73):73ra21. [PMID 21389265]
4. Krueger A. New carbon materials: biological applications of functionalized nanodiamond materials. Chemistry 2008;14(5):1382–90. [PMID 18033700]

Intellectual Property: HHS Reference No. E–175–2012/0—US Provisional Application No. 61/672,996 filed 18 Jul 2012.

Related Technology: HHS Reference No. E–261–2012/0—US Provisional Application No. 61/711,702 filed 09 Oct 2012, ''Imaging Methods and Computer-Readable Media for Background-Free imaging of Fluorescent Nanodiamonds.''

Licensing Contact: Michael Shmilovich; 301–435–5019; *shmilovm@mail.nih.gov*.

Collaborative Research Opportunity: The NHLBI Laboratory of Single Molecule Biophysics is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize fluorescent nanodiamonds for use as in vivo and in vitro optical tracking probes. For collaboration opportunities, please contact Keir C. Neuman, Ph.D. at neumankc@mail.nih.gov or 301–496–3376.

Dated February 20, 2013.

Richard U. Rodriguez,

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

[FR Doc. 2013–04443 Filed 2–26–13; 8:45 am]

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.

FOR FURTHER INFORMATION CONTACT: 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.

Chimeric Antigen Receptors to CD22 for Treating Hematological Cancers

Description of Technology: Chimeric antigen receptors (CARs) are hybrid proteins consisting of an antibody binding fragment fused to protein signaling domains that cause T-cells which express the CAR to become cytotoxic. Once activated, these cytotoxic T-cells can selectively eliminate the cells which they recognize via the antibody binding fragment of the CAR. Thus, by engineering a T-cell to express a CAR that is specific for a certain cell surface protein, it is possible to selectively target those cells for destruction. This is a promising new therapeutic approach known as adoptive cell therapy.

CD22 is a cell surface protein that is expressed on a large number of B-cell lineage hematological cancers, such as leukemia and lymphoma. Several promising therapies are being developed which target CD22, including therapeutic antibodies and immunotoxins. This technology concerns the use of a high affinity antibody binding fragment to CD22 (known as m971), as the targeting moiety of a CAR. The resulting CAR can be used in adoptive cell therapy treatment for cancer.

Potential Commercial Applications:
- Treatment of diseases associated with increased or preferential expression of CD22
- Specific diseases include hematological cancers such as chronic lymphocytic leukemia (CLL), hairy cell leukemia (HCL) and pediatric acute lymphoblastic leukemia (ALL)

Competitive Advantages:
- High affinity of the m971 antibody binding fragment increases the likelihood of successful targeting
- Targeted therapy decreases non-specific killing of healthy, essential cells, resulting in fewer non-specific side-effects and healthier patients
- Hematological cancers are susceptible to cytotoxic T-cells for treating because they are present in the bloodstream
- Expression of CD22 only on mature cells allows the avoidance of stem cell elimination during treatment

Development Stage: Pre-clinical.

Inventors: Rimas J. Orentas et al. (NCI).

Intellectual Property: HHS Reference No. E–291–2012/0—US Provisional Application No. 61/717,960 filed 24 Oct 2012.

Related Technology: HHS Reference No. E–080–2008/0—U.S. Patent Application No. 12/934,214 filed 23 Sep 2010.

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

Modified Peptide Nucleic Acids (PNAs) for Detection of DNA or RNA and Identification of a Disease or Pathogen

Description of Technology: The NIH announces a novel method for fast, simple, and accurate detection of nucleic acids outside the modern laboratory. Nucleic acid testing is highly specific and often provides definitive

identification of a disease or pathogen. Methods to detect nucleic acid sequences and identify a disease or pathogen are dominated by PCR, but applying PCR-based techniques in remote settings is challenging. Researchers at the NIH have developed a universal, colorimetric, nucleic acid-responsive diagnostic system that uses two short peptide nucleic acid (PNA) probes and does not rely on PCR. The design of a cyclopentane-modified surface probe and a biotin-containing reporter probe allows excellent DNA and RNA detection. NIH researchers have specifically demonstrated this technology's suitability for early detection of HIV RNA or anthrax DNA.

Potential Commercial Applications:

- Ultra-high sensitive detection of nucleic acids
- Convenient, universal, colorimetric diagnostic tool
- Can be used to detect any kind of infectious disease by simply changing the PNA sequences of the specific probe
- Suitable for early detection of HIV, anthrax, tuberculosis, human papilloma virus (HPV), avian flu, E. coli, and more

Competitive Advantages:

- Eliminates requirement for PCR
- Fast, simple method that can be used outside the laboratory
- Modified PNAs provide resistance to degradation by enzymes and a high degree of stability to any diagnostic device

Development Stage:

- Prototype
- In vitro data available

Inventors: Daniel Appella (NIDDK), Christopher Micklitsch (NIDDK), Chao Zhao (NIDDK), Bereket Oquare (ImClone Systems, Inc.).

Publication: Micklitsch CM, et al. Cyclopentane-Peptide nucleic acids for qualitative, quantitative, and repetitive detection of nucleic acids. Anal Chem. 2013 Jan 2;85(1):251–7. [PMID 23214925].

Intellectual Property: HHS Reference No. E–260–2012/0—US Application No. 61/684,354 filed 17 Aug 2012.

Licensing Contact: Charlene Sydnor, Ph.D.; 301–435–4689; *sydnorc@mail.nih.gov*.

Collaborative Research Opportunity: The NIDDK is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize Modified Peptide Nucleic Acids (PNAs) for Detection of DNA or RNA. For collaboration opportunities, please contact Cindy K. Fuchs, J.D. at *Cindy.Fuchs@nih.hhs.gov* or 301–451–3636.

Novel Vaccine for Prevention and Treatment of Chlamydia Infection

Description of Technology: The invention provides novel vectors, attenuated pathogens, compositions, methods and kits for preventing and/or treating chlamydia infections.

Chlamydia trachomatis is an obligate intracellular human pathogen with a unique biphasic developmental growth cycle. It's the etiological agent of trachoma, the world's leading cause of preventable blindness and the most common cause of bacterial sexually transmitted disease. *C. trachomatis* isolates maintain a highly conserved plasmid and naturally occurring plasmidless clinical isolates are rare, implicating its importance in chlamydial pathogenesis. Understanding the plasmid's role in chlamydial pathogenesis at a molecular level is an important objective for the future control of chlamydial infections. The NIAID inventor had studied chlamydia strains in both non-human primate and murine infectious models providing evidence that plasmids play an important role in chlamydial pathogenesis. In addition, the study results of macaque model of trachoma supports the use of plasmid-deficient organisms as novel live-attenuated chlamydial vaccines.

Potential Commercial Applications: Novel live-attenuated chlamydial vaccines.

Competitive Advantages:

- Virulence attenuated vectors that can be used as vaccines against chlamydia.
- Combination of vector with attenuated pathogenic agent improves the stability and replicative capacity of the pathogen.
- Features nucleic acids, attenuated pathogens, compositions, methods and kits to treat and prevent chlamydia infections.

Development Stage:

- Prototype
- In vitro data available
- In vivo data available (animal)
- In vivo data available (human)

Inventor: Harlan D Caldwell (NIAID).

Publications:

1. Song L, et al. The Chlamydia trachomatis plasmid-encoded Pgp4 is a transcriptional regulator of virulence associated genes. Infect Immun. 2013 Jan 14 (Epub ahead of print). [PMID 23319558]

2. Kari L, et al. A live-attenuated chlamydial vaccine protects against trachoma in nonhuman primates. J Exp Med. 2011 Oct 24;208(11):2217–23. [PMID 21987657]

Intellectual Property: HHS Reference No. E–133–2012/0—US Provisional Application No. 61/753,320 filed 16 Jan 2013

Licensing Contact: John Stansberry, Ph.D.; 301–435–5236; *stansbej@mail.nih.gov*

Collaborative Research Opportunity: The NIAID Laboratory of Intracellular Parasites is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize chlamydia vaccine. For collaboration opportunities, please contact Harlan D. Caldwell, Ph.D. at *hcaldwell@niaid.nih.gov.*

A High-Throughput Assay for Detection and Monitoring of Endocrine-Disrupting Chemicals in Water Sources

Description of Technology: This technology describes a high-throughput, fluorescence-based method to detect endocrine-disrupting chemicals (EDCs) in water sources.

There is growing awareness that a wide variety of synthetic and natural compounds that may lead to adverse health effects are present in water sources, such as streams, wells, and ground water; however, these compounds are often difficult to measure and thus are not commonly monitored. Even low concentrations of these compounds are of concern, as they may have biological effects at concentrations of parts per billion (PPB) or less. The presence of EDCs in the environment, in particular, is under examination for potential adverse effects on human health and on wildlife, such as cancer, immune suppression, impaired fertility, and increased incidence of diabetes and obesity.

Inventors at NCI have discovered a novel assay methodology for detecting endocrine EDCs in contaminated water. The assay utilizes fluorescently-labeled nuclear receptors in a high-throughput, cell-based format, and has the capability to detect very low concentrations of EDCs in water or other liquid samples. The inventors have already demonstrated proof of concept for this technology by using this assay to test for the presence of glucocorticoid and androgen receptor disruptors in water samples from 14 U.S. states, and also plan future studies for other types of EDCs. A product or service based on this technology could fulfill an unmet need for a high-throughput, rapid method for screening water samples for contaminants with potential endocrine-disrupting effects.

Potential Commercial Applications: Product or service for screening and detection of endocrine disrupting chemicals (EDCs) in samples from water sources and waste water.

Competitive Advantages:

- Rapid results—one day or less from sample retrieval to result
- Detects very low concentrations of EDCs
- Readily adaptable for use with a variety of endocrine receptor targets
- High-throughput format allows testing of many samples at once, with multiple types of endocrine receptor targets
- Tests for activity rather than a specific chemical, therefore can detect many variants modified in the environment

Development Stage:

- Prototype
- In vitro data available

Inventors: Gordon L. Hager and Diana A. Stavreva (NCI)

Publication: Stavreva D, et al. Prevalent Glucocorticoid and Androgen Activity in US Water Sources. Sci Rep. 2012;2:937. [PMID 23226835]

Intellectual Property: HHS Reference No. E–269–2011/0—US Provisional Application No. 61/656,473 filed 06 Jun 2012

Licensing Contact: Tara Kirby, Ph.D.; 301–435–4426; *tarak@mail.nih.gov*

Collaborative Research Opportunity: The NCI Laboratory of Receptor Biology & Gene Expression is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize Detection and Monitoring of Endocrine-Disrupting Chemicals in Water Sources. For collaboration opportunities, please contact John Hewes, Ph.D. at *hewesj@mail.nih.gov.*

Novel Diagnostic Marker for Prediction of Clearance of Hepatitis C Virus Infection

Description of Technology: One of the unfortunate aspects of hepatitis C virus (HCV) infection is that the majority of infected individuals will develop a chronic HCV infection. The current treatment for HCV infection involves direct acting antiviral drugs, such as HCV protease inhibitors, with or without pegylated IFN-alpha/ribavirin. Not all patients respond to treatments and the treatments themselves can cause severe adverse effects. The subject invention (*IFNL4-deltaG*) is a novel genetic polymorphism in the newly discovered *Interferon Lambda 4* (*IFNL4*) gene, which is located near the *IFNL3* (former *IL28B*) gene. The *IFNL4-deltaG* polymorphism can predict the likelihood of whether or not a patient will respond to treatment of HCV and, possibly, of other diseases treated with IFN-alpha (or other interferons). In particular, *IFNL4-deltaG* was found to be a better predictor of clinical outcome for IFN-alpha based treatment in people of African descent than the currently available diagnostic test (‘*IL28B’* genotype, defined by rs12979860 located within first intron of *IFNL4*). The predictive value of the *IFNL4-deltaG* polymorphism for response to IFN-alpha based treatment in HCV-infected Caucasians and Asians is comparable to current diagnostics. In addition, *IFNL4-deltaG* can predict the likelihood of a whether a person who is acutely infected with HCV infection will spontaneously clear the infection or develop chronic infection. As with treatment outcome, among individuals of African ancestry, genotype for *IFNL4-deltaG* is a better predictive marker for spontaneous clearance of HCV than ‘*IL28B’* genotype, while providing similar predictive value in individuals of European or Asian descent.

Potential Commercial Applications:

- Diagnostic for prediction of patient response to HCV treatment
- Diagnostic for prediction of patient response to treatment with IFN-alpha (or other interferons)
- Diagnostic tool for prediction of spontaneous clearance of HCV infection

Competitive Advantages:

- Better than current ‘IL28B’ based diagnostics for predicting response to IFN-alpha based HCV treatments for people of African descent.
- Comparable predictive capabilities to current ‘IL28B’ based diagnostics for response to IFN-alpha based HCV treatments in Caucasians and Asians.

Development Stage:

- Early-stage
- Pre-clinical
- In vitro data available

Inventors: Liudmila Prokunina (NCI), Thomas R. O’Brien (NCI), Brian P. Muchmore (NCI), Raymond P. Donnelly (FDA)

Publication: Prokunina-Olsson L, et al. A variant upstream of IFNL3 (IL28B) creating novel interferon gene IFNL4 is associated with impaired clearance of hepatitis C virus. Nat Genet. 2013 Feb;45(2):164–71. [PMID 23291588]

Intellectual Property: HHS Reference No. E–217–2011/0—

- U.S. Provisional Patent Application No. 61/543,620 filed 05 Oct 2011
- International PCT Application No. PCT/US2012/59048 filed 05 Oct 2012

Related Technology: HHS Reference No. E–217–2011/1—U.S. Provisional Patent Application No. 61/616,664 filed 28 Mar 2012

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

Collaborative Research Opportunity: The NCI Division of Cancer Epidemiology & Genetics, Laboratory of Translational Genomics, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize development of a gene-based test to be used in the clinic. For collaboration opportunities, please contact John Hewes, Ph.D. at *hewesj@mail.nih.gov.*

Novel Host Target for Treatment of Hepatitis C Virus Infection

Description of Technology: The subject technology is a newly discovered Interferon-lambda 4 (IFNL4) protein found through analysis of genomic data derived from primary human hepatocytes, molecular cloning and functional annotation. The IFNL4 protein is related to but distinct from other know IFNs and its expression is inducible in conditions that mimic viral infection. Preliminary studies indicate that this protein may play a role in impaired natural and treatment induced clearance of HCV. These findings suggest that the protein can potentially be a new target for treating HCV infection.

Potential Commercial Applications:

- Novel target for treatment of HCV infection.
- Diagnostics can be developed for detection of IFNL4 mRNA or protein.
- Existing biological reagents for detection of IFNL4—expression assays, antibodies and protein.

Competitive Advantages: IFNL4 is created by a genetic variant *IFNL4-deltaG,* which is present only in a subset of individuals, suggesting that IFNL4 is not an essential protein and its functional inactivation may be well-tolerated.

Development Stage:

- Early-stage
- Pre-clinical
- In vitro data available

Inventors: Liudmila Prokunina (NCI), Thomas R. O’Brien (NCI), Brian P. Muchmore (NCI), Raymond P. Donnelly (FDA)

Publication: Prokunina-Olsson L, et al. A variant upstream of IFNL3 (IL28B) creating novel interferon gene IFNL4 is associated with impaired clearance of hepatitis C virus. Nat Genet. 2013 Feb;45(2):164–71. [PMID 23291588]

Intellectual Property: HHS Reference No. E–217–2011/1—U.S. Provisional Patent Application No. 61/616,664 filed 28 Mar 2012

Related Technology: HHS Reference No. E–217–2011/0—

- U.S. Provisional Patent Application No. 61/543,620 filed 05 Oct 2011

- International PCT Application No. PCT/US2012/59048 filed 05 Oct 2012

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

Collaborative Research Opportunity: The NCI Division of Cancer Epidemiology & Genetics, Laboratory of Translational Genomics, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize development of tools for detection of IFNL4 mRNA and protein and modulation of its function. For collaboration opportunities, please contact John Hewes, Ph.D. at *hewesj@mail.nih.gov.*

Brachyury-Directed Vaccine for the Prevention or Treatment of Cancers

Description of Technology: Tumor invasion and metastasis are the primary drivers of cancer-related mortality. Therapies that have an ability to specifically target invasive and/or metastatic cells are anticipated to have a significant impact in the clinical management of advanced cancers.

Researchers at the NIH have developed a vaccine technology that stimulates the immune system to selectively destroy metastasizing cells. Brachyury, a master transcription factor that governs the epithelial-mesenchymal transition, was shown to be significantly overexpressed in primary and metastasizing tumors relative to normal human tissues. Stimulation of T cells with the Brachyury peptide promoted a robust immune response and the targeted lysis of invasive tumor cells. Brachyury overexpression has been demonstrated in a range of human tumors (breast, lung, colon and prostate, among others) suggesting that a therapeutic vaccine derived from this technology would be broadly applicable for the treatment of cancer.

Potential Commercial Applications:

- Preventative cancer vaccine for patients with precancerous lesions of the breast, colon or prostate.
- Therapeutic cancer vaccine for the treatment of disseminated and late-stage tumors.
- Vaccine component of a multi-modal cancer therapy.

Competitive Advantages:

- Treatment targets invasive and metastatic tumor cells which are the primary cause of cancer-related mortality.
- Vaccine can eliminate cancer stem cells which are resistant to conventional therapies.
- Compatible with the clinically-proven TRICOM cancer vaccine platform.
- Available (Optimized) for use with non-pox, non-yeast vectors including: Adenovirus, lentivirus, etc., and for use with protein- or peptide-based vaccines.

Development Stage:

- Pre-clinical
- In vitro data available
- In vivo data available (animal)
- In vivo data available (human)

Inventors: Claudia Palena and Jeffrey Schlom (NCI)

Publications:

1. Fernando RI, et al. The T-box transcription factor Brachyury promotes epithelial-mesenchymal transition in human tumor cells. J Clin Invest. 2010 Feb;120(2):533–44. [PMID 20071775]
2. Palena C, et al. The human T-box mesodermal transcription factor Brachyury is a candidate target for T-cell-mediated cancer immunotherapy. Clin Cancer Res. 2007 Apr 15;13(8):2471–8. [PMID 17438107]

Intellectual Property: HHS Reference No. E–055–2011/0—US Application No. 61/701,525 filed 14 Sep 2012

Licensing Contact: Sabarni Chatterjee, Ph.D.; 301–435–5587; *chatterjeesa@mail.nih.gov*

Collaborative Research Opportunity: The National Cancer Institute Laboratory of Tumor Immunology and Biology is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize Brachyury-directed cancer vaccine technology. For collaboration opportunities, please contact John D. Hewes, Ph.D. at *hewesj@mail.nih.gov.*

Novel Plasmid Vectors for the Soluble Expression of Recombinant Proteins in Escherichia coli

Description of Technology: A series of novel plasmid vectors for the soluble expression and subsequent purification of recombinant proteins that have historically proven to be extremely difficult to purify from *Escherichia coli* (*E. coli*) are provided. Because of its ease of growth and generally low cost to cultivate, *E. coli* is often employed as the host for vectors expressing recombinant proteins. In an ideal situation, the recombinant protein is expressed from a strong promoter, highly soluble, and recovered in high yield and activity. Unfortunately, it is quite common that the overproduced recombinant protein is either detrimental to the cell or simply compartmentalized into insoluble inclusion bodies. Recently, NIH investigators have developed plasmid vectors that enable the recovery and purification of recombinant proteins that have previously proven to be difficult to express in soluble form. These vectors have a pSC101 origin of replication and, therefore, are maintained in *E. coli* at approximately five (5) copies per cell (plasmid details and maps will be provided upon request). These vectors express the recombinant proteins at low basal levels and this feature facilitates higher solubility and correct folding of the expressed protein. The utility of these vectors is verified by expressing and purifying full-length human DNA polymerases from *E. coli* and showing that the purified DNA polymerases are catalytically active *in vitro.*

Potential Commercial Applications: The expression vectors described here can be used to:

(a) obtain recombinant proteins that were previously hard to purify,
(b) produce recombinant proteins from a number of sources and with different catalytic activities, and
(c) express multimeric protein complexes.

Competitive Advantages: The expression vectors described here:

(a) dramatically increase the proportion of soluble protein that can be obtained in *E. coli,*
(b) fully compatible with the replicons of conventional high-expression systems (e.g., pET vectors, EMD Biosciences, and
(c) facilitate the correct folding of the recombinant protein and increases its solubility.

Development Stage:

- Prototype
- Early-stage
- In vitro data available

Inventors: Roger Woodgate, John P. McDonald, and Karata Kiyonobu (NICHD)

Publication: Frank EG, et al. A strategy for the expression of recombinant proteins traditionally hard to purify. Anal Biochem. 2012 Oct 15;429(2):132–9. [PMID: 22828411]

Intellectual Property: HHS Reference No. E–028–2010/0—Research Tools. Patent protection is not being pursued for this technology.

Licensing Contact: Suryanarayana (Sury) Vepa, Ph.D., J.D.; 301–435–5020; *vepas@mail.nih.gov*

Dated: February 21, 2013.

Richard U. Rodriguez,

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

[FR Doc. 2013–04481 Filed 2–26–13; 8:45 am]

BILLING CODE 4140–01–P