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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.

FOR FURTHER INFORMATION: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804; telephone: 301-496-7057; fax: 301-402-0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Therapeutic RNA Switches and Auto-recognizing Therapeutic R/DNA Chimeric Nanoparticles (NP) for HIV Treatment

Description of Technology: RNA interference (RNAi) as a therapeutic agent is routinely used to knock down the expression of target genes in diseased cells. Using siRNAs it is possible to knock down target mRNA expression. It is possible, for example, to induce cell death through co-RNAi by simultaneously targeting several human anti-apoptotic genes with different siRNAs. NIH inventors computationally and experimentally developed a new technology that utilizes two (or more) cognate RNA/DNA NPs that, when recombined within the cell, trigger the RNAi pathway as well as other functionalities that exist inside diseased cells. This new methodology therefore opens a new route in the development of auto-recognizing "smart" nucleic acids based nanoparticles for a wide range of applications in biomedical RNA nanotechnology. This new approach may overcome several issues commonly associated with the clinical delivery of siRNA, such as intravascular degradation, the potential for immune-mediated toxicities, tissue specificity and pharmacodynamics.

Potential Commercial Applications:

• Therapeutics that control gene expression (e.g., anti-apoptotic genes)

• Combinations with other therapeutics to treat cancer, RNA viruses (e.g., HIV) and other RNA related diseases

• Triggered release of siRNAs within cells

• Research on targeting cells

• Labeling of targeted cells

• Research on cancer cells harboring cancer and other RNA related diseases in patients

• Research on treatment of RNA related viruses

Competitive Advantages:

• Size overcomes problems with traditional siRNA pharmacokinetics

• Chemical stability improves half-life

• Incorporation of multiple functionalities split and otherwise

• Multi-stage delivery controls activation

Development Stage:

• Prototype

• In vitro data available

Inventors: Bruce A. Shapiro (NCI), Eckart HU Bindewald (NCI), Kirill A. Afonin (NCI), Arti Santhanam (NCI), Mathias Viard (SAIC), Luc Jaeger (UCSB)

Intellectual Property: HHS Reference No. E-038-2012/0 — Research Material. Patent protection is not being pursued for this technology.

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

Collaborative Research Opportunity: The NCI Center for Cancer Research Nanobiology Program is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize this technology to advance antiviral therapy concepts. For collaboration opportunities, please contact John Hewes, Ph.D. at hewesj@mail.nih.gov.

Multilayer X-Ray Transmission Grating Array for Phase-Contrast Imaging and Tomography

Description of Technology: Classical X-ray Computed Tomography (CT) and radiography are based on X-ray absorption and cannot show soft tissue structures as well as Magnetic Resonance Imaging (MRI). Detecting the phase delay/advance of X-rays that travel through the body could enhance soft tissue contrast 10 - 100 times. Submicron-period X-ray transmission gratings for medical x-ray energies can substantially enhance the phase detection sensitivity, but fabrication is a great challenge. This invention includes a method to fabricate multilayer transmission gratings of large areas. The design uses multilayer deposition of alternating materials on a staircase substrate to form micro grating arrays of extremely small periods and high aspect ratio in large areas. This invention should substantially improve the visibility of soft tissue structures and reduce radiation dose to patients.

Potential Commercial Applications:

• X-ray diagnostic imaging

• X-ray non-destructive materials testing

• X-ray security screening

• X-ray lithography of nanostructures

• Also applies to neutron beam or proton beam imaging

Competitive Advantages:

• Gratings of ultra-high aspect ratio and small period allow phase-contrast imaging at high x-ray energies which are suitable for human body CT, and provide better soft tissue contrast in radiography and CT

• Reduces radiation exposure to patient

• Large area gratings enable full field imaging without raster or line scanning

Development Stage:

• Pre-clinical

• Early-stage

Inventor: Han Wen (NHLBI)

Publication: Lynch SK, et al. Multilayer-coated micro-grating array for x-ray phase-contrast imaging. Proc. SPIE 8076, 80760F (2011); http://dx.doi.org/10.1117/12.888939.

Intellectual Property: HHS Reference No. E-207-2011/0 — U.S. Provisional Application No. 61/578,719 filed 21 Dec 2011

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

Collaborative Research Opportunity: The Imaging Physics Lab, Biophysics and Biochemistry Center, NHLBI/NIH, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize multilayer-coated gratings for phase-contrast CT. For collaboration opportunities, please contact Dr. Han Wen at wenh@nhlbi.nih.gov.

Human DNA Polymerase Gamma for Testing the Effect of Drugs on Mitochondrial Function

Description of Technology: One of the primary means for treating HIV infection is the use of antiviral nucleotide or nucleoside analogs. These analogs work by

inhibiting the activity of reverse transcriptase, the enzyme responsible for preparing the HIV genome for integration into the DNA of the host cell. Although these analogs do not have an effect on the polymerases responsible for replicating the human genome, the polymerase responsible for replicating the mitochondrial genome is sensitive to these analogs. When patients are exposed to nucleotide or nucleoside analogs through long-term treatment regimens, the replication of the mitochondrial genome can be adversely affected. Since mitochondrial functionality is necessary for cell activity, the nucleotide and nucleoside analogs can cause serious and unwanted side-effects.

This invention concerns the cloning and purification of human DNA polymerase gamma, the polymerase responsible for replicating the mitochondrial genome. The enzymes that have been purified include the wild-type version, a version which lacks exonuclease (proofreading) activity, and several versions with modified activity due to the mutation of the enzyme. These purified enzymes can be used to directly test the effects of new drugs that affect the activity of polymerases, such as nucleotide and nucleoside analogs.

Potential Commercial Applications:

• Research reagent to screen the effects of antiviral drugs (nucleotide and nucleoside analogs) on mitochondrial function

• Research reagent to test the mitochondrial toxicity of other drugs that can affect polymerase activity

Competitive Advantages:

• Purified polymerase allows for direct analysis of the effect of nucleotide analogs on DNA polymerase gamma

• Different formats of the enzyme such as the exonuclease-deficient version, allows comprehensive testing of drug candidates

Development Stage: In vitro data available

Inventors: William Copeland et al. (NIEHS)

Publication: Longley MJ, et al. Characterization of the native and recombinant catalytic subunit of human DNA polymerase gamma: identification of residues critical for exonuclease activity and dideoxynucleotide sensitivity. Biochemistry. 1998 Jul 21;37(29):10529-39. [PMID 9671525]

Intellectual Property: HHS Reference Nos. E-191-2011/0, B-035-1998/0, and B-035-1998/1 — Research Materials. Patent protection is not being pursued for these technologies.

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

Collaborative Research Opportunity: The NIEHS is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize the antibodies. For collaboration opportunities, please contact Elizabeth Denholm at denholme@niehs.nih.gov.

Biomarker to Predict High-risk Clinical Outcomes for Colon, Lung, and Ovarian Cancers

Description of Technology: It has long been known that general genomic instability is associated with cancer. NIH scientists Drs. Habermann and Reid at the National Cancer Institute, along with West Virginia University scientists Drs. Mettu and

Guo, have recently identified specific genes whose instability is strongly associated with poor outcomes for colon, small-cell lung, and ovarian cancers. Using this 12-gene genomic instability signature as a biomarker could be diagnostic tool for identifying high-risk patients that would benefit from more aggressive forms of treatment.

Potential Commercial Applications: Diagnostic tool for identifying patients at high-risk for developing colon, small-cell lung, and ovarian cancers that are recurring and/or aggressive.

Competitive Advantages:

• Allows more accurate prognoses by separating high-risk from low-risk cancer patient populations.

• Allows doctors to choose more individualized therapies for patients based on whether the cancer is at high or low risk for aggressiveness or recurrence.

Development Stage: Clinical

Inventors: Thomas K. Ried (NCI) et al.

Intellectual Property: HHS Reference No. E-119-2011/0 — PCT Application No. PCT/US2011/061871 filed 22 Nov 2011

Licensing Contact: Surekha Vathyam, Ph.D.; 301-435-4076; vathyams@mail.nih.gov

Isolation of Hybridomas Producing Monoclonal Antibodies (MAbs) Inhibitory to Human CYP2J2

Description of Technology: The National Institutes of Health announces three specific monoclonal antibodies that strongly inhibit and/or immunoblot the human cytochrome P450 2J2 (CYP2J2).

Cytochrome P450s catalyze the NADPH-dependent oxidation of arachidonic acid to various eicosanoids found in several species. The eicosanoids are biosynthesized in numerous tissues including pancreas, intestine, kidney, heart and lung where they are involved in many different biological activities.

MAb 6-5-20-8 selectively inhibits CYP2J2-mediated arachidonic acid metabolism by more than 80% and also immunoblots the enzyme. MAb 6-2-16-1 also selectively inhibits arachidonic acid metabolism by more than 80% but does not immunoblot the enzyme. MAb 5-3-2-2 is not inhibitory but selectively immunoblots the enzyme. These antibodies can be used to identify and quantify inter-individual variation in physiological functions and to study pharmacological drug metabolism in various tissues.

Potential Commercial Applications:

• These antibodies can be used to identify and quantify inter-individual variation in physiological functions.

• These antibodies can be used to study pharmacological drug metabolism in various tissues.

Competitive Advantages: These antibodies strongly inhibit and/or immunoblot the human cytochrome P450 2J2 (CYP2J2).

Development Stage: In vitro data available

Inventors: Darryl C. Zeldin (NIEHS) et al.

Publications:

1. Wu S, et al. Molecular cloning and expression of CYP2J2, a human cytochrome P450 arachidonic acid epoxygenase highly expressed in heart. J Biol Chem. 1996 Feb 16;271(7):3460-8. [PMID 8631948]

2. Node K, et al. Anti-inflammatory properties of cytochrome P450 epoxygenase-derived eicosanoids. Science 1999 Aug 20;285(5431):1276-9. [PMID 10455056]

3. Node K, et al. Activation of Galpha s mediates induction of tissue-type plasminogen activator gene transcription by epoxyeicosatrienoic acids. J Biol Chem. 2001 May 11;276(19):15983-9. [PMID 11279071]

4. Zeldin DC. Epoxygenase pathways of arachidonic acid metabolism. J Biol Chem. 2001 Sep 28;276(39):36059-62. [PMID 11451964]

5. Yang B, et al. Overexpression of cytochrome P450 CYP2J2 protects against hypoxia-reoxygenation injury in cultured bovine aortic endothelial cells. Mol Pharmacol. 2001 Aug;60(2):310-20. [PMID 11455018]

6. King LM, et al. Cloning of CYP2J2 gene and identification of functional polymorphisms. Mol Pharmacol. 2002 Apr;61(4):840-52. [PMID 11901223]

7. Sun J, et al. Inhibition of vascular smooth muscle cell migration by cytochrome p450 epoxygenase-derived eicosanoids. Circ Res. 2002 May 17;90(9):1020-7. [PMID 12016269]

Intellectual Property: HHS Reference No. E-337-2003/0 — Research Material. Patent protection has not been pursued for this technology.

Licensing Contact: Fatima Sayyid, M.H.P.M.; 301-435-4521; Fatima.Sayyid@nih.hhs.gov

Collaborative Research Opportunity: The NIEHS is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize this antibody. For collaboration opportunities, please contact Elizabeth Denholm at denholme@niehs.nih.gov.

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Date

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