DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, DHHS.

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.

Carbohydrate-Encapsulated Quantum Dots for Cell-Specific Biological Imaging

Joseph Barchi, Sergei Svarovsky (NCI).
U.S. Provisional Application filed 22 Mar 2004 (DHHS Reference No. E–133–2004/0–US–01).
Licensing Contact: Michael Shmilovich; 301/435–5019; *shmilovm@mail.nih.gov*.

Available for licensing is intellectual property covering carbohydrate-encapsulated quantum dots (QD) for use in medical imaging and methods of making the same. Certain carbohydrates, especially those included on tumor glycoproteins are known to have affinity for certain cell types. One notable glycan used in the present invention is the Thomsen-Freidenreich disaccharide (Ga1β1–3Ga1NAα–O–Ser/Thr) that is readily detectable in 90% of all primary human carcinomas and their metastases. These glycans can be exploited for medical imaging. Quantum Dots (QDs) are metallic (CdSe or CdTe) nanoparticles with detectable luminescent properties. Conjugating luminescent QDs with target specific glycans permits efficient imaging of the tissue to which the glycans bind with high affinity. Accurate imaging of diseased cells (*e.g.*, primary and metastatic tumors) is of primary importance in disease management. The inventors describe the only stable synthesis of glycan encapsulated QDs. In one embodiment, the synthesis involves the preparation of hybrid QDs containing a glycan and a luminescence-enhancing passivating agent in various ratios. Second generation QDs contain the glycan ligands and polyethylene glycols (PEG) of varying chain lengths. The PEG modifications produced QDs that maintained high luminescence while reducing non-specific cell binding.

MVL, an Antiviral Protein From a Cyanobacterium

Carole A. Bewley (NIDDK).
DHHS Reference No. E–068–2004/0–US–01 filed 08 Mar 2004.
Licensing Contact: Sally Hu; 301/435–5606; *hus@mail.nih.gov*.

The invention describes the discovery of the carbohydrate binding protein (lectin), MVL, that binds specifically to oligosaccharides comprising the tetrasaccharide, Manα(1→6)(Manβ(1→4)G1cNAcβ(1→4)G1cNAc, with very high (nanomolar) affinity.

In particular, this invention shows that the binding of MVL to the carbohydrate residues of the glycoprotein gp120 can block HIV fusion into human cells and thus inhibit HIV infection. As a consequence, subject invention may be used in the development of therapeutics for the treatment of retroviral infections, such as AIDS. In addition, MVL described in this invention may also have particular value when used in combination treatments with other antiviral therapies directed at other viral targets, such as protease and reverse transcriptase.

Multiplex Real-Time PCR

Enrique Zudaire Ubani, Frank Cuttitta (NCI).
U.S. Patent Application No. 10/658,602 filed 08 Sep 2003 (DHHS Reference No. E–215–2003/0–US–01).
Licensing Contact: Cristina Thalhammer-Reyero; 301/435–4507; *thalhamc@mail.nih.gov*.

This invention is in the field of multiplex real-time polymerase chain reaction (PCR). In particular, the invention pertains to the quantification of multiple amplicons in a single polymerase chain reaction based on the different melting temperatures of amplicons. A utility U.S. Patent Application No. 10/658,602 was filed on September 8, 2003.

PCR is a primer-directed *in vitro* reaction for the enzymatic amplification of a fragment of DNA, involving repetitive cycles of DNA template denaturation, primer annealing to the DNA template, and primer extension. The result is an exponential accumulation of a specific DNA fragment or amplicon from an initial nominal amount of sample DNA templates. Multiplex PCR offers a more efficient approach to PCR, whereby multiple pairs of primers are used to simultaneously amplify multiple amplicons in a single PCR reaction. The simultaneous amplification of various amplicons decreases both the cost and turn-around time of PCR analysis, minimizes experimental variations and the risk of cross-contamination, and increases the reliability of end results. Multiplex PCR has gained popularity in many areas of DNA testing, including prognosis, diagnostic, gene deletion analysis, mutation and polymorphism analysis, genotyping and DNA array analysis, RNA detection, farmacogenomics and identification of microorganisms.

Real-time PCR has been developed to overcome limitations in quantifying amplicons during an ongoing PCR reaction, since traditional PCR and multiplex PCR are often limited to a qualitative analysis of end-product amplicons. Real-time PCR is based on the principles that emission of fluorescence from dyes directly or indirectly associated with the formation of newly synthesized amplicons or the annealing of primers with DNA templates can be detected and is proportional to the amount of amplicons in each PCR cycle. The resulting emission curve can then be used to calculate the initial copy number of a nucleic acid template at the beginning of the PCR reaction. Real-time PCR eliminates the need for post PCR steps and is highly recognized for its high sensitivity, precision and reproducibility. This invention is directed to methods for real-time monitoring and quantification of multiple amplicons in a single multiplex real-time PCR reaction based on the use of a double stranded DNA dye and the melting temperature discrepancy among the amplicons.

Methods and Compositions for the Inhibition of HIV–1 Replication

Sharon M. Wahl, Nancy Vazquez-Maldonado, Teresa Greenwell-Wild (NIDCR).
U.S. Provisional Application No. 60/516,794 filed 04 Nov 2003 (DHHS Reference No. E–114–2003/0–US–01).
Licensing Contact: Sally Hu; 301/435–5606; *hus@mail.nih.gov*.

This invention relates to methods and compositions for the attenuation of HIV–1 replication in human cells, and especially in human macrophages by targeting a host cell protein. HIV–1 infected macrophages typically resist cell death, support viral replication, and facilitate HIV–1 transmission. We found that the gene encoding cyclin-dependent kinase inhibitor 1A (CDKN1A) is consistently expressed following virus binding, and re-expressed at the peak of HIV–1 replication. The protein encoded by this gene, also known as p21, is associated with cell cycle regulation, anti-apoptotic response and cell differentiation. Increased levels of p21 may enhance survival and long-term persistence of HIV–1 infected macrophages. Treatment of cultured infected cells with antisense p21 oligonucleotides or p21 short interfering RNA (p21 siRNA) significantly reduced replication of HIV–1. A similar effect was observed when infected cells were exposed to the synthetic triterpenoid CDDO, a potent multifunctional agent that influences differentiation and has anti-inflammatory and anti-proliferative properties, including inhibition of p21. Neither p21 oligonucleotides nor CDDO were toxic to the cultured macrophages. Thus, p21 inhibitors could be safe and effective anti-HIV therapeutic candidates to be used in conjunction with current anti-retroviral therapy.

Cannula for Pressure Mediated Drug Delivery

Stephen Wiener, Robert Hoyt, John Deleonardis, Randal Clevenger, Robert Lutz, Brian Safer (NHLBI).

PCT Application No. PCT/US99/11277 filed 21 May 1999, which published as WO 99/59666 on 25 Nov 1999 (DHHS Reference No. E–196–1998/2–PCT–01); U.S., Australian, Japanese, and European rights pending.

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

Available for licensing are methods and devices for selectively delivering therapeutic substances to specific histological or microanatomical areas of organs (*e.g.*, introduction of the therapeutic substance into a hollow organ space such as the hepatobiliary duct or the gallbladder lumen) at a controlled pressure, volume and/or rate which allows the substance to reach a predetermined cellular layer. The volume or flow rate of the substance can be controlled so that the intralumenal pressure reaches a predetermined threshold beyond which subsequent subepithehal delivery of the substance occurs. Alternatively, a lower pressure is selected that does not exceed the threshold level, so that delivery occurs substantially to the epithelial layer. Such site-specific delivery of therapeutic agents permits localized delivery in concentrations that may otherwise produce systemic toxicity. Occlusion of venous or lymphatic drainage from the organ can also help prevent systemic administration of therapeutic substances, and increases selective delivery to superficial epithelial cellular layers. Delivery of genetic vectors can also be delivered to target cells. The access device comprises a cannula with a wall piercing tracar within the lumen. Two axially spaced inflatable balloons engage the wall securing the cannula and sealing the puncture site. A catheter equipped with an occlusion balloon is guided through the cannula to the location where the therapeutic substance is to be delivered.

Dated: April 22, 2004.

Steven M. Ferguson,

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

[FR Doc. 04–9685 Filed 4–28–04; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Cancer Institute; Notice of Closed Meeting

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 meeting.

The meeting 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 Cancer Institute Review Group, Subcommittee G—Education.

Date: June 16–18, 2004

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

Agenda: To review and evaluate grant applications.

Place: Sheraton Suites Alexandria, 801 North Saint Asaph Street, Alexandria, VA 22314.

Contact Person: Ilda M. Mckenna, Scientific Review Administrator, Research Training Review Branch, Division of Extramural Activities, National Cancer Institute, 6116 Executive Boulevard Room 8111, Bethesda, MD 20892, (301) 496–7481, *mckennai@mail.nih.gov*.

(Catalogue of Federal Domestic Assistance Program Nos. 93.392, Cancer Construction; 93.393, Cancer Cause and Prevention Research; 93.394, Cancer Detection and Diagnosis Research 93.395, Cancer Treatment Research; 93.396, Cancer Biology Research; 93.397, Cancer Centers Support; 93.398, Cancer Research Manpower; 93.399, Cancer Control, National Institutes of Health, HHS)

Dated: April 21, 2004.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 04–9682 Filed 4–28–04; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Cancer Institute; Notice of Closed Meeting

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 meeting.

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Name of Committee: National Cancer Institute Initial Review Group; Subcommittee F—Manpower & Training.

Date: June 14–15, 2004.

Time: 8:30 a.m. to 3 p.m.

Agenda: To review and evaluate grant applications.

Place: Holiday Inn Georgetown, 2101 Wisconsin Avenue, NW., Washington, DC 20007.

Contact Person: Lynn M. Amende, PhD, Scientific Review Administrator, Resources and Training Review Branch, Division of Extramural Activities, National Cancer Institute, National Institutes of Health, 6116 Executive Boulevard Room 8105, Bethesda, MD 20892, 301–451–4759, *amendel@mail.nih.gov*.

(Catalogue of Federal Domestic Assistance Program Nos. 93.392, Cancer Construction; 93.393, Cancer Cause and Prevention Research; 93.394, Cancer Detection and Diagnosis Research; 93.395, Cancer Treatment Research; 93.396, Cancer Biology