The recent clinical introduction of small molecule inhibitors that target single molecules as effective anticancer therapies underscores the potential of patient specific therapeutic interventions. However, the definition of a cancer specific target need not be a single transforming or survival-related gene or gene product. Another targetable and relatively irreversible cellular state might be the complexity and instability of the chromosomal complement of cancer cells. Structural and numerical chromosomal alterations are present in most neoplasms and karyotypic complexity is associated with a poor clinical prognosis as well as aggressive and distinctive histopathologic features.

The present invention describes methods for the selecting candidate compounds for evaluation for the treatment of cancer by defining the karyotypic complexity and heterogeneity in human cancer cells based on three components of genomic anatomy: ploidy, numerical chromosome changes, and structural chromosome rearrangements. Measures of complexity include the number of chromosomal rearrangements present in a cell line (structural complexity, SC) and the number of chromosome deviations from the ploidy level (numerical complexity, NC). Measures of cell-to-cell chromosomal variability, which reflect the degree of ongoing instability, include numerical heterogeneity (NH) and structural heterogeneity (SH). Utilizing the methods claimed in the this application, a number of chemical compounds were identified and later determined to have increased cytotoxicity toward cancer cell lines with a specific karyotypic complexity.

The positive correlations between drug sensitivity and karyotypic complexity and heterogeneity found in this analysis (122 statistically significant positive correlations) provide a distinct opportunity to identify agents that are more active against karyotypically complex and chromosomally unstable cancer cells. Such cells would typically be found in the epithelial cancers, which cause so much therapeutic concern and frustration.

Inhibition of Human Papillomavirus Type 16 and 18 E6 and E7 Oncogene Expression by E6 and E7-Specific siRNAs

Zhi-Ming Zheng (NCI).
DHHS Reference No. E–079–2005/0–US–01.
Licensing Contact: Michelle A. Booden; (301) 451–7337; *boodenm@mail.nih.gov*.

Cervical infection with human papillomaviruses (HPVs), such as HPV16 and HPV18, is strongly associated with development of cervical cancer. Integration of the viral genomes into the cervical cell genome is characteristic of infection with these HPVs. Thus, the majority of cervical cancer cells isolated from patients carry these viral genomes and express two viral oncoproteins, E6 and E7, which induce p53 and pRb degradation. Importantly, expression of both E6 and E7 oncogenes is essential for survival of cervical cancer cells.

Small interfering RNA (siRNA) is emerging as a powerful tool for gene silencing and has much potential for anticancer and antiviral applications. The present invention describes a method employing novel siRNA sequences for inhibiting expression of the E6 and E7 viral oncoproteins of HPV 16 and 18, which are required for development and progression of HPV mediated cervical cancer.

Since HPV 16 and HPV 18 are the most prevalent HPV types inducing cervical cancer in women, this discovery may have a significant impact on cervical cancer therapy. This technology could also have additional implications in variety of HPV-associated indications, such as anogenital warts, bladder, and head and neck carcinomas.

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

Biomarkers for Osteoarthritis

Shari M. Ling *et al.* (NIA).
U.S. Provisional Application No. 60/602,334 filed 18 Aug 2004 (DHHS Reference No. E–354–2004/0–US–01).
Licensing Contact: Marlene Shinn-Astor; (301) 435–4426; *shinnm@mail.nih.gov*.

Osteoarthritis is chronic, often progressive and substantially disabling condition that becomes more common with advanced age. Osteoarthritis commonly involves the knees, hands, hips, neck and back resulting in pain and limitations of movement.

Unfortunately clinically available tests are neither capable of detecting osteoarthritis early in its development, nor sensitive enough to adequately assess disease progression. A better means of diagnosing early osteoarthritis and its progression that can be used to assess the response to therapeutic treatments is needed. The currently available laboratory techniques are highly sensitive but either lack specificity or require large volumes of sample. Rolling Circle Amplification (RCA) is new technology that precisely localizes unique signals arising from single reporter molecules. RCA has been incorporated into antibody-based microarray system protein chips that enable testing with high sensitivity and specificity for hundreds of proteins simultaneously, using small sample volumes.

This invention describes a method of using RCA technology for detecting the expression of serum proteins that are perturbed in osteoarthritis patients. The results of this testing can be used to identify proteins associated with osteoarthritis presence, prediction of osteoarthritis development and prognosis, predict response to osteoarthritis treatment and potentially also identify future anti-osteoarthritic drugs.

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

Water-Soluble, Antineoplastic Derivatives of Taxol

Rudiger D. Haugwitz *et al.* (NCI).
U.S. Patent 4,942,184 issued 17 Jul 1990 (DHHS Reference No. E–090–1987/0–US–01).
Licensing Contact: John Stansberry; 301/435–5236; *stansbej@mail.nih.gov*.

A new class of taxol derivatives offer an improved method for treating certain cancers. The use of taxol as an antineoplastic agent has been limited due to poor solubility in aqueous solutions. These new taxol derivatives have improved water solubility while retaining the cytotoxic properties of the parent compounds. Their method of synthesis and use in treating cancer patients are provided.

Dated: March 7, 2005.

Steven M. Ferguson,

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

[FR Doc. 05–5081 Filed 3–14–05; 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, 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.

CpG Oligonucleotide Prodrugs

Daniela Verthelyi, Serge Beaucage, Andrzej Grajkowski (FDA).

U.S. Provisional Patent Application filed 13 Dec 2004 (DHHS Reference No. E–215–2004/0–US–01).

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

Available for licensing and commercial development into prodrugs and methods of synthesizing the same are CpG oligonucleotides that include thermolabile substituent on at least one nucleotide. The invention also provides compositions that include carriers and therapeutically effective amounts of at least one CpG oligonucleotide prodrug. Therapeutic methods of using such thermolabile CpG oligonucleotide prodrugs are also provided (*e.g.*, a prodrug that elicits an immune response). The thermolabile substituent is typically bonded to the non-bridging oxygen atom of at least one phosphate or phosphorothioate in the oligonucleotide.

The thermolabile CpG oligonucleotide prodrugs of the present invention can be administered to a patient as a prodrug of the parent CpG oligonucleotides *in vivo.* The thermolabile CpG oligonucleotide prodrugs of the present invention are rapidly internalized by immune cells (B cells, macrophages, dendritic cells, and monocytes) and localized in endocytic vesicles where they can interact with Toll-like receptor 9. This interaction triggers an immunostimulatory cascade characterized by B-cell proliferation, dendritic cell maturation, natural killer cell activation and the secretion of a variety of cytokines, chemokines and polyreactive immunoglobulins. Administration of the thermolabile CpG oligonucleotide prodrugs of the present invention to a host, for example, can improve the resistance of the host against infectious pathogenic microorganisms, *e.g.*, parasites, bacteria, and viruses.

Identification of Proteins in a Genome

James L. Hartley, Dominic Esposito, and Kelly Jeanne Stanard (SAIC/NCI).

U.S. Provisional Application No. 60/628,948 filed 19 Nov 2004 (DHHS Reference No. E–161–2004/0–US–01).

Licensing Contact: Cristina Thalhammer-Reyero; (301) 435–4507; *thalhamc@mail.nih.gov.*

Available for licensing and commercial development are methods for identifying soluble proteins in a sample. Identification and characterization of bioactive compounds is a critical step in drug discovery, and there is a need for improved methods for identifying soluble proteins. One method provided, which produces soluble deletion derivatives of a protein, includes the steps of incubating a vector with a nucleic acid sequence encoding the protein, flanked by a first and second site-specific recombination sites, in the presence of one or more transposons with a third and fourth site-specific recombination sites and a transposase protein, to insert the one or more transposons into the vector, followed by transfer to further vectors with additional site-specific recombination sites, which are propagated, isolated, combined and recombined in the presence of a recombinase. A second method is for identifying two or more soluble proteins and includes the steps of expressing two or more vectors with the nucleic acid sequence encoding a soluble protein operatively linked to a promoter in one or more cells, and identifying and quantifying the isolated two or more soluble proteins by mass spectroscopy. The above methods can be used alone or in combination. These methods will enable researchers to identify both individual protein targets of drugs, as well as protein families or protein signaling pathways, thereby enhancing drug development.

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

An Epitope-Enhancement of Human CD4 HIV Epitope

Jay A. Berzofsky (NCI), Takahiro Okazaki (NCI).

U.S. Provisional Application No. 60/567,073 filed 30 Apr 2004 (DHHS Reference No. E–076–2004/0–US–01).

Licensing Contact: Robert M. Joynes; (301) 594–6565; *joynesr@mail.nih.gov.*

This invention relates to an epitope of the HIV–1 envelope protein recognized by a $CD4^+$ T cell line that was developed from immunization with canarypox vectors expressing gp120 of HIV–1. Virus-specific $CD4^+$ T cell help and $CD8^+$ cytotoxic T cell responses are critical for the maintenance of effective immunity in chronic viral infections. The importance of the $CD4^+$ T cell has been documented in HIV infection. A T1-specific $CD4^+$ T cell line from a healthy volunteer immunized with a canarypox vector expressing gpl20 has been developed. This T1-specific $CD4^+$ T cell line was restricted to DR13, which is common in the U.S. in both Caucasians and African-Americans and is one of the major haplotypes in Africans. The present invention provides isolated polypeptides comprising an enhanced T1 epitope. Amino acid substitutions in the T1 epitope were made to induce a stronger epitope-specific $CD4^+$ T cell response than the original epitope resulting in an improved CD4 epitope (also designated an epitope enhancement). A polypeptide comprising the enhanced CD4 epitope can be used as a component in composition either alone or in combination with other adjuvants and other immunogenic compositions to provide a more effective immune response to HIV infection.

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.

CC Chemokine Receptor 5 DNA, New Animal Models and Therapeutic Agents for HIV Infection

C. Combadiere, Y. Feng, E.A. Berger, G. Alkahatib, P.M. Murphy, C.C. Broder, P.E. Kennedy (NIAID);

U.S. Provisional Application No. 60/018,508 filed 28 May 1996 (DHHS Reference No. E–090–1996/0–US–01);

U.S. Patent Application No. 08/864,458 filed 28 May 1997 (DHHS Reference No. E–090–1996/0–US–04);

U.S. Patent Application No. 10/439,845 filed 15 May 2003 (DHHS Reference No. E–090–1996/0–US–05);

U.S. Patent Application No. 10/700,313 filed 31 Oct 2003 (DHHS Reference No. E–090–1996/0–US–06);

U.S. Patent Application No. 10/846,185 filed 14 May 2004 (DHHS Reference No. E–090–1996/0–US–07);

PCT Application No. PCT/US97/09586 filed 28 May 1997 (DHHS Reference No. E–090–1996/0–PCT–02);
European Patent Application No. 97929777.7 filed 28 May 1997 (DHHS Reference No. E–090–1996/0–EP–03).
Licensing Contact: Peter Soukas; (301) 435–4646; *soukasp@mail.nih.gov.*

Chemokine receptors are expressed by many cells, including lymphoid cells, and function to mediate cell trafficking and localization. CC chemokine receptor 5 (CCR5) is a seven-transmembrane, G protein-coupled receptor (GPCR) which regulates trafficking and effector functions of memory/effector T-lymphocytes, macrophages, and immature dendritic cells. Chemokine binding to CCR5 leads to cellular activation through pertussis toxin-sensitive heterotrimeric G proteins as well as G protein-independent signalling pathways. Like many other GPCR, CCR5 is regulated by agonist-dependent processes which involve G protein coupled receptor kinase (GRK)-dependent phosphorylation, beta-arrestin-mediated desensitization and internalization.

Human CCR5 also functions as the main coreceptor for the fusion and entry of many strains of human immunodeficiency virus (HIV–1, HIV–2). HIV–1 transmission almost invariably involves such CCR5-specific variants (designated R5); individuals lacking functional CCR5 (by virtue of homozygosity for a defective CCR5 allele) are almost completely resistant to HIV–1 infection. Specific blocking of CCR5 (*e.g.* with chemokine ligands, anti-CCR5 antibodies, CCR5-blocking low MW inhibitors, etc.) inhibits entry/infection of target cells by R5 HIV strains. Cells expressing CCR5 and CD4 are useful for screening for agents that inhibit HIV by binding to CCR5. Such agents represent potential new approaches to block HIV transmission and to treat infected people. A small animal expressing both human CCR5 along with human CD4 supports entry of HIV into target cells, a necessary hurdle that must be overcome for development of a small animal model (*e.g.* transgenic mouse, rat, rabbit, mink) to study HIV infection and its inhibition.

The invention embodies the CCR5 genetic sequence, cell lines and transgenic mice, the cells of which coexpress human CD4 and CCR5, and which may represent valuable tools for the study of HIV infection and for screening anti-HIV agents. The invention also embodies anti-CCR5 agents that block HIV env-mediated membrane fusion associated with HIV entry into human CD4-positive target cells or between HIV-infected cells and uninfected human CD4-positive target cells.

This technology was reported in Alkhatib *et al.*, ''CC CKR5: a RANTES, MIP–1alpha, MIP–1beta receptor as a fusion cofactor for macrophage-tropic HIV–1,'' Science 272:1955–1958 (1996). The technology is available for exclusive or nonexclusive licensing.

Dated: March 7, 2005.

Steven M. Ferguson,

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

[FR Doc. 05–5082 Filed 3–14–05; 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/or contract proposals 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 and/or contract proposals, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Cancer Institute Special Emphasis Panel, Loan Repayment Program: OD04–060 (Clinical) & OD04–061 (Pediatric).

Date: April 4, 2005.

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

Agenda: To review and evaluate grant applications and/or proposals.

Place: National Institutes of Health, 6116 Executive Boulevard, Rockville, MD 20852.

Contact Person: Bratin K. Saha, PhD, Program Coordination and Referral Branch, Division of Extramural Activities, National Cancer Institute, 6116 Executive Blvd., Bethesda, MD 20892, (301) 402–0371, *sashab@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: March 8, 2005.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 05–5074 Filed 3–14–05; 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.

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 Initial Review Group, Subcommittee D—Clinical Studies.

Date: April 6–8, 2005.

Time: 6 p.m. to 1 p.m.

Agenda: To review and evaluate grant applications.

Place: Holiday Inn Select Bethesda, 8120 Wisconsin Ave., Bethesda, MD 20814.

Contact Person: William D. Merritt, PhD, Scientific Review Administrator, Research Programs Review Branch, National Cancer Institute, Division of Extramural Activities, 6116 Executive Blvd., 8th Floor, Bethesda, MD 20892–8328, 301–496–9767, *wm63f@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: March 8, 2005.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 05–5075 Filed 3–14–05; 8:45 am]

BILLING CODE 4140–01–M