Dated: August 26, 2005.

Scott Gottlieb,

Deputy Commissioner for Policy.

[FR Doc. 05–17470 Filed 9–1–05; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Proposed Collection: Comment Request; Extension of OMB No. 0925–0417/exp. 08/31/05, Responsibility of Applicants for Promoting Objectivity in Research for Which Public Health Service Funding Is Sought and Responsible Prospective Contractors—42 CFR Part 50, Subpart F

Summary: In compliance with the requirement of Section 3507(a)(1)(D) of the Paperwork Reduction Act of 1995, the Office of the Director (OD), Office of Extramural Research (OER), the National Institutes of Health (NIH) has submitted to the Office of Management and Budget (OMB) a request for review and approval of the information collection listed below. Proposed information collection was previously published in the **Federal Register** on May 12, 2005, Volume 70, No. 91, page 25095 and allowed 60 days for public comment. No public comments were received. The purpose of this notice is to allow an additional 30 days for public comment. The National Institutes of Health may not conduct or sponsor, and the respondent is not required to respond to, an information collection that has been extended, revised, or implemented on or after October 1, 1995, unless it displays a currently valid OMB control number.

Proposed Collection: Title: Responsibility of Applicants for Promoting Objectivity in Research for Which Public Health Service Funding Is Sought and Responsible Prospective Contractors—42 CFR Part 50, Subpart F; *Type of Information Collection Request:* Extension, OMB 0925–0417, Expiration Date 8/31/05. *Need and Use of Information Collection:* This is a request for OMB approval for the information collection and recordkeeping requirements contained in the final rule 42 CFR Part 50 Subpart F and Responsible Contractors: 45 CFR Part 94. *Frequency of response:* On occasion. *Affected Public:* Individuals or households; business or other for-profit; not-for-profit institutions; and State, Local or Tribal Government. *Type of Respondents:* Any public or private entity or organization. The annual reporting burden is as follows: *Estimated Number of Respondents:* 42,800; *Estimated Number of Responses per Respondent:* 1.60; *Average Burden Hours Per Response:* 3.40; and *Estimated Total Annual Burden Hours Request:* 232,000.

Request for Comments: Written comments and/or suggestions from the public and affected agencies are invited on one or more of the following points: (1) Whether the proposed collection of information is necessary for the proper performance of the function of the agency, including whether the information will have practical utility; (2) the accuracy of the agency's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on those who are to respond, including the use of appropriate automated, electronic, mechanical, or other technological collection techniques or other forms of information technology.

Direct Comments to OMB: Written comments and/or suggestions regarding the item(s) contained in this notice, especially regarding the estimated public burden and associated response time should be directed to the Office of Management and Budget, Office of Regulatory Affairs, New Executive Office Building, Room 10235, Washington, DC 20503, Attention: Desk Officer for NIR. To request more information on the proposed project or to obtain a copy of the data collection plans and instruments, contact Ms. Diane Dean, Division of Grants Policy, Office of Policy for Extramural Research Administration, NIH, Rockledge 1 Building, Room 3525, 6705 Rockledge Drive, Bethesda, MD 20892–7974, or call non-toll-free number 301–435–0930, or E-mail your request, including your address to: *hahnm@od.nih.gov.*

Comments Due Date: Comments regarding this information collection are best assured of having their full effect if received within 30 days of the date of this publication.

Dated: August 25, 2005.

Charles Mackay,

Chief, Project Clearance Branch, OPERA, OER, National Institutes of Health.

[FR Doc. 05–17458 Filed 9–1–05; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing: Selected Technologies From the NIH Cancer Therapeutics Portfolio

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 contacting George G. Pipia, Ph.D., Technology Licensing Specialist, Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852; telephone: 301/435–5560; fax: 301/402–0220; e-mail: *pipiag@mail.nih.gov.* A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Antitumor Macrocyclic Lactones

Michael R. Boyd (NCI).

U.S. Patent No. 6,353,019 issued 05 Mar 2002 (HHS Reference No. E–244–1997/0–US–07) and related foreign patent applications.

Vacuolar-Type (H+)-ATPase-Inhibiting Compounds and Uses Thereof

Michael R. Boyd (NCI).

U.S. Patent Application No. 09/914,708 filed 31 Aug 2001 (HHS Reference No. E–244–1997/3–US–06) and related foreign patent applications.

This technology covers a broad composition of matter which includes the salicylihalamides, lobatamides, and numerous other structurally related small molecules which have been shown to inhibit mammalian vacuolar ATPase at low nanomolar concentrations. The compounds are also potent inhibitors of cancer cell growth, with particular specificity for melanoma, osteosarcoma and selected lung, colon and CNS tumor cell lines. Experimental tumor and pharmacokinetic studies are underway

to select the most effective analogs for further development. The potential of these compounds to inhibit invasion and metastasis to bone sites is also under investigation.

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

Novel 2-Alkoxy Estradiols and Derivatives Thereof

Ravi Varma (NCI), *et al.*
U.S. Patent No. 6,136,992 issued 24 Oct 2000 (HHS Reference No. E–188–1998/1–US–01).

The present invention is directed to novel 2-alkoxy estradiols and derivatives of 2-alkoxy estradiols having anticancer activity as claimed in the U.S. Patent 6,136,992. The invention is also directed to methods of preparing these novel compounds. These compounds have improved activity against a wide variety of tumor cell lines, including lung, colon, central nervous system, melanoma, ovarian, renal, prostate and breast cancers, compared with 2-methoxy estradiols. It is expected that these compounds will be very useful in the treatment of a wide variety of cancers. In addition, the present compounds have a low affinity for the estrogen receptor and are, therefore, expected to have fewer side effects than estradiols.

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

A Combined Growth Factor-Deleted and Thymidine Kinase-Deleted Vaccinia Virus Vector for Cancer Therapy

J. Andrea McCart (NCI), David L. Bartlett (NCI), and Bernard Moss (NIAID).
U.S. Patent Application No. 09/991,721 filed 13 Nov 2001, claiming priority to 28 May 1999 (HHS Reference No. E–181–1999/0–US–05).

Tumor-selective, replicating viruses may infect and kill cancer cells and efficiently express therapeutic genes in cancer cells. The current invention embodies mutant vaccinia virus expression vectors. These vectors, which are vaccinia virus growth factor-deleted and thymidine-kinase deleted, are substantially incapable of replicating in non-dividing cells, and as such have specificity for cancer cells. It is therefore believed that the vectors will be of value for cancer therapy either by directly killing cancer cells or by expressing therapeutic agents in cancer cells while sparing normal, non-dividing cells.

This research is described, in part, in: E. Chang *et al.*, ''Targeting vaccinia to solid tumors with local hyperthermia,'' *Hum Gene Ther.* 2005 Apr, 16(4):435–44; J.A. McCart, ''Oncolytic vaccinia virus expressing the human somatostatin receptor SSTR2: molecular imaging after systemic delivery using 111In-pentetreotide,'' *Mol Ther.* 2004 Sep, 10(3):553–61; H.J. Zeh, ''Development of a replication-selective, oncolytic poxvirus for the treatment of human cancers,'' *Cancer Gene Ther.* 2002 Dec, 9(12):1001–12; J.A. McCart, ''Systemic cancer therapy with a tumor-selective vaccinia virus mutant lacking thymidine kinase and vaccinia growth factor genes,'' *Cancer Res.* 2001 Dec 15, 61(24):8751–7.

SH2 Domain Binding Inhibitors

Terrence R. Burke, Jr., *et al.* (NCI).
U.S. Patent Application No. 10/362,231 filed 22 Aug 2001, claiming priority to 22 Aug 2000 (HHS Reference No. E–262–2000/0–US–03).
U.S. Patent Application No. 10/517,717 filed 17 Mar 2005, claiming priority to 28 Jun 2002 (HHS Reference No. E–262–2000/1–US–03).

Signal transduction processes underlie the transfer of extracellular information to the interior of the cell and ultimately to the nucleus. A variety of signal transduction processes are critical for normal cellular homeostasis, with protein-tyrosine kinases (PTKs) playing central roles in many of these pathways. Examples of such PTKs include the PDGF receptor, the FGF receptor, the HGF receptor, members of the EGF receptor family, such as the EGF receptor, erb-B2, erb-B3 and erb-B4, the src kinase family, Fak kinase and the Jak kinase family. Protein-tyrosine phosphorylation that results from the action of PTKs can modulate the activity of certain target enzymes as well as facilitate the formation of specific multi-protein signaling complexes through the actions of homologous protein modules termed Src homology 2 (SH2) domains, which recognize specific phosphotyrosyl containing sequences. A malfunction in this system through tyrosine kinase overexpression and/or deregulation can be manifested by various oncogenic and hyperproliferative disorders, including cancers, inflammation, autoimmune disease, hyperproliferative skin disorders, psoriasis and allergy/asthma, etc. The disclosed compounds, *e.g.* peptides, preferably, macrocyclic peptides, are Grb2 SH2 domain signaling antagonists with enhanced binding affinity. The claims of the current application are directed to compositions of matter and methods of use which provide for the diagnosis, testing and treatment of the aforementioned disease states.

SH2 Domain Binding Inhibitors

Terrence R. Burke, Jr., *et al.* (NCI).
U.S. Provisional Application No. 60/504,241 filed 18 Sep 2003 (HHS Reference No. E–315–2003/0–US–01).
U.S. Patent Application No. 10/944,699 filed 17 Sep 2004 (HHS Reference No. E–315–2003/0–US–02).

The present invention provides for ultra-potent Grb2 SH2 domain-binding compounds, or a pharmaceutically acceptable salt thereof. The compounds of the present invention represent tetrapeptide mimetics whose conformation is constrained through macrocyclization. Low picomolar binding affinity is achieved in in vitro Grb2 SH2 domain binding assays. Addition of the covered agent to the extracellular media of erbB–2 over-expressing breast cancer cells at low nanomolar concentrations results in effective intracellular blockade of Grb2 association with activated cytoplasmic erbB–2 tyrosine kinase. Antimitogenic effects are observed in erbB–2-dependent breast cancer cells in culture at sub-micromolar concentrations. The present invention further provides a pharmaceutical composition comprising a pharmaceutically or pharmacologically acceptable carrier and a compound of the present invention. The present invention also provides a method for inhibiting an SH2 domain from binding with a phosphoproteins comprising contacting an SH2 domain with a compound of the present invention. The present invention also provides a method of preventing or treating a disease, state, or condition by the use of the compound. While the invention has been described and disclosed below in connection with certain embodiments and procedures, it is not intended to limit the invention to those specific embodiments. Rather it is intended to cover all such alternative embodiments and modifications as fall within the spirit and scope of the invention.

This research is described, in part, in: Z. Shi *et al.*, ''A novel macrocyclic tetrapeptide mimetic that exhibits low-picomolar Grb2 SH2 domain-binding affinity,'' Biochem. Biophys. Res. Commun. (2003 Oct 17) 310(2):378–383, doi:10.1016/j.bbrc.2003.09.029; Z. Shi *et al.*, ''Synthesis of a 5-methylindolyl-containing macrocycle that displays ultrapotent Grb2 SH2 domain-binding

affinity,'' J. Med. Chem. (2004 Feb 12) 47(4):788–791, doi:10.1021/jm030440b.

A New Approach Toward Macrocyclization of Peptides

Terrence R. Burke, Jr., *et al.* (NCI).
U.S. Provisional Application No. 60/614,800 filed 30 Sep 2004 (HHS Reference No. E–327–2004/0–US–01).

The invention relates to cyclic peptides for use as inhibitors of oncogenic signal transduction for cancer therapy. The current invention discloses novel cyclic peptides resulting from ring closure between the alpha and beta positions of C-terminal and N-terminal residues, respectively. This allows retention of key functionality needed for binding to target proteins, which results in increased affinity.

Cyclic peptides that retain key chemical functionality may be of particular importance in inhibiting oncogenic signaling cascades for therapeutic benefit. In many oncogenic signal transduction cascades, tyrosine protein kinases phosphorylated target proteins. Propagation of the signal is achieved when these phosphorylated tyrosyl residues are bound by proteins bearing SH2 domains. Cyclic peptides that disrupt the interaction between proteins with SH2 domains and proteins with phosphorylated tyrosyl residues could block oncogenic signals and serve as powerful cancer therapeutic agents. As several moieties are required for optimal recognition by SH2 domains, the cyclic peptides of the current invention could be more effective inhibitors of SH2 domain proteins, or of other proteins where increased specificity is desired. The inventors have determined that the peptides of the current invention bind to the Grb2-SH2 domain with high affinity, supporting their potential use as therapeutic agents. The current invention is related to U.S. Provisional Application No. 60/504,241 (HHS Reference No. E–315–2003/0–US–01).

Conjugates of Ligand, Linker, and Cytotoxic Agent and Related Compositions and Methods of Use

Nadya Tarasova, Christopher J. Michejda, Marcin Dyba, Carolyn Cohran (NCI).
U.S. Patent Application No. 10/505,239 filed 19 Aug 2004, claiming priority to 27 Feb 2002 (HHS Reference No. E–057–2002/2–US–02).

Systemic toxicity of drugs is one of the most serious problems in cancer chemotherapy and frequently is dose limiting. Specific delivery of cytotoxic drugs to cancer cells remains among the most intractable problems of cancer therapy. Targeted delivery of anti-proliferation drugs through the cell surface receptors that are over expressed on cancer cells can reduce systemic toxicity and increase effectiveness of a treatment.

The present invention describes cytotoxic compounds with an intracellular target that can selectively enter tumor cells through specific receptors on the cell surface. The invention also describes a conjugate comprising a cytotoxic agent, a linker arm and a ligand capable of delivering a cytotoxic agent in a cell specific manner. Such conjugates of a cytotoxic agent and a ligand (delivery moiety) have increased selectivity for tumor cells. The toxic moiety and the ligand are joined by a linker arm that is stable in circulation, but is easily cleaved in lysosomes upon internalization of the conjugate. A panel of compounds comprised of a variety of cytotoxic warheads, against various intracellular targets linked to an assortment of ligands, has been developed and tested in a model system. Ligand moieties of these conjugates are capable of specific delivery of cytotoxic agents to receptors that are frequently over expressed in gastric, colon, lung, breast, ovarian and pancreatic tumors. These compounds have the potential to be highly effective anti-tumor agents with considerably little negative effect. This disclosed technology could provide new and exciting methodologies to treat cancer.

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

DNA-Binding Polyamide Drug Conjugates

Zoltan Szekely, Humcha K. Hariprakasha, Marek W. Cholody, Christopher J. Michejda (NCI).
U.S. Patent Application No. 10/506,085 filed 01 Oct 2004, claiming priority to 27 Feb 2002 (HHS Reference No. E–060–2002/2–US–02).

Many current anti-cancer drugs have the DNA of cancer cells as their principal target. However, in most instances, the drugs are not selective and are plagued by toxicities, which are frequently dose limiting. The present invention seeks to enhance anti-tumor selectivity and decrease unspecific toxicity. It has been known that various polyamides can target the minor groove of DNA, and rules have been devised to ascertain the sequence-reading properties of the component residues of the polyamide chain. The present invention utilizes sequence-selective polyamide technology together with groups that modify DNA, either by sequence-selective alkylation or strand cleavage. The DNA-modifying moieties that are used for this purpose are novel derivatives based on the cyclopropylbenzindole (CBI) core structure. These compounds alkylate the DNA only when bound into the minor groove, and they provide some DNA-sequence recognizing capability of their own. The DNA-modifying agents are either embedded in the polyamide chain as components of the chain or are located at the termini. These compounds are highly toxic to cancer cells that over-express a targeted DNA sequence (*e.g.* the c-Myc oncogene promoter sequence) and are much less toxic to non-cancerous tissue. The compounds of the present invention represent a novel method for targeting DNA of cancer cells.

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

New Building Blocks for DNA Binding Agents

Zoltan Szekely *et al.* (NCI).
U.S. Provisional Application No. 60/508,543 filed 03 Oct 2003 (HHS Reference No. E–291–2003/0–US–01).
PCT Application No. PCT/US04/32617 filed 01 Oct 2004, which published as WO 2005/032594 on 14 Apr 2005 (HHS Reference No. E–291–2003/0–PCT–02).

There remains a need for therapeutic conjugates that have improved antitumor selectivity and nucleic acid sequence-binding specificity. Ideally such conjugates will have fewer side effects and lower cytotoxicity to healthy cells and tissues. The knowledge of the geometry of conjugates allows for a rational design of therapeutic conjugates, ones that have increased specificity of binding to a minor groove of the DNA, while maintaining maximum activity of the alkylating subgroup of the conjugates. The present invention provides such conjugates. The conjugates of the present invention bind to the minor grove of DNA in a sequence-specific manner and deliver an alkylating moiety to a specific site on the DNA. The present invention provides a pharmaceutical composition comprising a pharmaceutically or pharmacologically acceptable carrier and compounds of the present invention. The present invention also provides a method of preventing or treating a disease or condition by the use of the compound. The NIH inventors currently are testing the conjugates in in-vitro assay and are

starting pre-clinical studies of the conjugates using animal cancer models.

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

Maleiimide Anti-Tumor Phosphatase Inhibitors

Christopher J. Michejda *et al.* (NCI).
U.S. Provisional Application No. 60/546,841 filed 22 Feb 2004 (HHS Reference No. E–110–2004/0–US–01).
PCT Application No. PCT/US05/05742 filed 22 Feb 2005 (HHS Reference No. E–110–2004/0–PCT–02).

The present invention describes novel phosphatase inhibitors that appear to target the CDC25 family of phosphatases. The new compounds have potent activity against human liver cancer cells in vitro and in vivo against an orthotopic liver cancer in rats. In tumor cells, these new inhibitors appear to target the phosphorylation status of several cell cycle proteins that are important for cell survival and thus could represent a novel class of chemotherapeutic agents targeting cancer cells.

2-Amino-O4-Substituted Pteridines and Their Use as Inactivators of O6-Alkylguanine-DNA Alkyltransferase

Robert C. Moschel *et al.* (NCI).
U.S. Provisional Application No. 60/534,519 filed 06 Jan 2004 (HHS Reference No. E–274–2003/0–US–01).
PCT Application No. PCT/US04/41577 filed 10 Dec 2004 (HHS Reference No. E–274–2003/0–PCT–02).

This invention is directed to 2-amino-O4-benzylpteridine derivatives targeted for use in cancer treatment in combination with chemotherapeutic agents such as 1,3-bis(2-chloroethyl)-1-nitrosurea (BCNU) or temozolomide. The derivatives of the present invention inactivate the O6-alkylguanine-DNA-alkyltransferase repair protein and thus enhance activity of such chemotherapeutic agents. Examples of these derivatives have advantages over the earlier O6-benzylguanine compounds from this research group. Some compounds of the current invention are more water soluble compared to O6-benzylguanine and they exhibit greater specificity for inactivating O6-alkylguanine-DNA-alkyltransferase in certain tumor cells, compared to normal cells.

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

Beta-Glucuronidase Cleavable Prodrugs of O6-Alkylguanine-DNA Alkyltransferase Inactivators

Robert C. Moschel *et al.* (NCI).
U.S. Provisional Application No. 60/608,045 filed 08 Sep 2004 (HHS Reference No. E–307–2004/0–US–01).

The present invention relates to prodrugs of inactivators of O6-alkylguanine-DNA alkyltransferase. The prodrugs are cleaved by the beta-glucuronidase enzyme found in tumor cells or co-administered to the patient, and the drugs are targeted for use in cancer treatment in combination with antineoplastic alkylating agent such as 1,3-bis(2-cloroethyl)-1-nitrosouria or temozolomide.

Identification of a Tricyclic Amino Amide (NSC–644221) Inhibitor of the Hypoxic Signaling Pathway

Giovanni Melillo (NCI).
U.S. Provisional Application No. 60/618,279 filed 12 Oct 2004 (HHS Reference No. E–185–2004/0–US–01).
U.S. Provisional Application No. 60/570,615 filed 12 May 2004 (HHS Reference No. E–185–2004/1–US–01).
PCT Application filed 11 May 2005 (HHS Reference No. E–185–2004/2–PCT–01).

This invention describes the identification of a tricyclic (1,4-dioxane) amino amide with confirmed potent activity in inhibiting HIF–1 transcriptional activity.

HIF–1 is a transcription factor and plays an important role in adaptation of cancer cells to an hypoxic environment. HIF–1 significantly increases the ability of cancer cells to survive under strenuous conditions. It contributes to the ability of cancer cells to migrate and invade surrounding tissue, and is important for the formation of new blood vessels that are essential for growth and metastasis of cancer cells. Thus HIF–1 mediates survival and spreading of cancer cells. Previous studies have shown that HIF–1 is also important in human cancers, and therefore, inhibition of HIF–1 activity is contemplated in the field as a therapy for cancer patients.

The inventors, using a cell-based high throughput screen, identified a new compound, NSC–644221, with potent inhibitory activity of the HIF–1 pathway. The compound inhibits expression of HIF–1 and reduces its accumulation in the cell. This compound also inhibits expression of endogenous genes that are under control of HIF–1, such as Vascular Endothelial Growth Factor (VEGF) that is essential for the formation of new blood vessels. Preliminary experiments in xenograft models have indicated that NSC–644221 reaches the tumor tissue when administered intraperitoneally and inhibits HIF–1-dependent luciferase expression in U251–HRE cells.

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

Inhibitors of the Protein Kinase Chk2 to Abrogate Apoptosis and Sensitize Cancer Cells to DNA Targeted Therapies

Yves Pommier *et al.* (NCI).
U.S. Provisional Application filed 29 Jul 2005 (HHS Reference No. E–211–2005/0–US–01).

Chk2 is a protein kinase activated in response to DNA double strand breaks. In normal tissues, Chk2 phosphorylates and thereby activates substrates that induce programmed cell death, or apoptosis, via interactions with p53, E2F1, PML proteins. In cancer tissues, where apoptosis is suppressed, Chk2 phosphorylates and inactivates cell cycle checkpoints (via interactions with Cdc25, phosphatases and Brca1 proteins), which allows cancer cells to repair and tolerate DNA damage. Hence, Chk2 inhibitors would be expected to protect normal tissues by reducing apoptosis, and to sensitize cancer cells to DNA-targeted agents.

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

Dated: August 25, 2005.

Steven M. Ferguson,

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

[FR Doc. 05–17457 Filed 9–1–05; 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