

Total Emission Detection System for Multi-Photon Microscopy

Description of Technology: Available for licensing and commercial development is a novel two-photon microscope system, which would allow improved fluorescent light collection, the use of less excitation power and deeper penetration of tissue and isolated cells. Multi-photon fluorescence microscopy (MPFM) is an imaging technique that can investigate biological processes to sub-cellular resolution at depths of hundreds of microns below the surface of biological tissues. MPFM provides higher resolution imaging of tissues than confocal imaging, but is currently limited by the use of inefficient light collection systems, which lead to detection of only a fraction of the light that is emitted from the sample. The new system consists of an array of mirrors, lenses, and reflecting surfaces designed to collectively maximize the probability of collecting all emitted fluorescent light to a detector, thereby providing enhanced brightness of light detected from the sample and an increase in signal-to-noise ratio (SNR). This increase in SNR can be used to improve time resolution, reduce laser power requirements and reduce photodynamic damage.

Applications: Three-dimensional imaging of biological tissues and cells; Three-dimensional imaging of semiconductor integrated circuits.

Market: Optical Imaging.

Development Status: Late-stage technology.

Inventors: Christian A. Combs, Robert S. Balaban, Jay R. Knutson (NHLBI).

Patent Status: U.S. Provisional Application No. 60/835,462 filed 04 Aug 2006 (HHS Reference No. E-257-2005/0-US-01).

Licensing Status: Available for exclusive or non-exclusive licensing.

Licensing Contact: Chekesha S. Clingman, Ph.D.; 301-435-5018; clingmac@mail.nih.gov

Collaborative Research Opportunity: The NHLBI Light Microscopy Core Facility is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize a total emission detection system for multi-photon imaging. Please contact Lili Portilla, Director of the NHLBI Office of Technology Transfer and Development at 301-402-5579 or via e-mail at LILIP@nih.gov for more information.

Dated: June 19, 2007.

Steven M. Ferguson,

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

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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.

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.

A Novel Discriminatory Small Peptide Inhibitor of Hsp90 Targeting Oncogenic Kinases

Description of Technology: Heat shock protein 90 (Hsp90) is a molecular chaperone required for stability and function for many proteins (clients). Presently, there are clinical trials focusing on small molecule Hsp90 inhibitors; however, pharmacologic Hsp90 inhibition causes destabilization, ubiquitination and proteasome-degradation of all client proteins indiscriminately.

Hsp90 was found to be overexpressed in tumor cells; thereby making Hsp90 a promising molecular target for cancer therapy. Additionally, some Hsp90-dependent client proteins (non-kinases) were identified as putative tumor suppressors, suggesting that indiscriminate degradation of all Hsp90 client proteins is not ideal. Finding a molecular inhibitor that discriminately

inhibits Hsp90 that would target only client kinase proteins would be an ideal therapeutic agent for cancer treatment.

The current invention is a short peptide that inhibits Hsp90 that prevents the recognition and function of client kinase proteins, and promotes the degradation of client kinase proteins, while not affecting other non-kinase client proteins.

Applications and Modality: Current applications include targeting client kinase proteins promoting degradation, and preventing recognition and function of the client kinase proteins; restriction of Hsp90 inhibition to client kinases that utilize similar Hsp90 recognition sequences to the oncogenic tyrosine kinase Hsp90 client ErbB2; and having kinase-specific chaperone inhibitors preferentially active as anti-cancer agents compared to indiscriminate pharmacologic inhibitors of Hsp90.

Market: 600,000 deaths from cancer related diseases were estimated in 2006; In 2006, cancer drug sales were estimated to be \$25 billion; There is a burgeoning drug market for Hsp90 inhibitors for cancer treatment.

Development Status: The technology is currently in the preclinical stage of development.

Inventors: Leonard M. Neckers et al. (NCI).

Patent Status: U.S. Provisional Application No. 60/895,313 filed 16 Mar 2007 (HHS Reference No. E-121-2007/0-US-01); U.S. Provisional Application No. 60/909,834 filed 03 Apr 2007 (HHS Reference No. E-121-2007/1-US-01).

Licensing Status: Available for exclusive and non-exclusive licensing.

Licensing Contact: Adaku Nwachukwu, J.D.; 301-435-5560; madua@mail.nih.gov.

Collaborative Research Opportunity: The NCI Urologic Oncology Branch is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize peptide inhibitor of Hsp90. Please contact John D. Hewes, Ph.D. at 301-435-3121 or hewesj@mail.nih.gov for more information.

A Novel Treatment for Non-Small Cell Lung Cancer Using Mesothelin-Targeted Immunotoxins

Description of Technology: Mesothelin is a glycoprotein, whose expression has been largely restricted to mesothelial cells in normal tissues, although epithelial cells of the trachea, tonsil, fallopian tube, and kidney have shown immunoreactivity. Mesothelin has been shown to be expressed in several cancers including pancreatic carcinomas, gastric carcinomas and

ovarian carcinomas, and has the potential of being used as a tumor marker and a novel target for the development of new treatments.

The technology relates to the finding that some non-small cell lung cancers (NSCLC) express the antigen mesothelin. Targeting the tumors with antibodies or immunotoxins that specifically bind mesothelin can be a potential new treatment for non-small cell lung cancer. The SSIP immunotoxin and its variants that specifically bind to mesothelin can be used for the treatment of NSCLC.

Applications and Modality: NSCLC can be treated by targeting mesothelin.

Advantage: Anti-mesothelin antibodies and immunotoxins are already available and being tested for several cancers.

Development Status: The technology is in pre-clinical stage of development.

Inventors: Ira H. Pastan (NCI) et al.

Patent Status: U.S. Provisional Application No. 60/891,923 filed 27 Feb 2007 (HHS Reference No. E-120-2007/0-US-01), entitled "Treatment of Non-Small Cell Lung Cancer with Mesothelin-Targeted Immunotoxins."

Licensing Status: Available for exclusive and non-exclusive licensing.

Licensing Contact: Jesse S. Kindra, J.D.; 301-435-5559; kindraj@mail.nih.gov

Collaborative Research Opportunity: The National Cancer Institute's Laboratory of Molecular Biology is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize anti-mesothelin antibodies and immunotoxins. Please contact John D. Hewes, Ph.D. at 301-435-3121 or hewesj@mail.nih.gov for more information.

A Gene Expression Profile That Predicts Ovarian Cancer Patient Response to Chemotherapy

Description of Technology: Ovarian cancer is a poor prognosis disease that remains the most lethal of all gynecologic malignancies. Warning symptoms do not occur until the tumor has already spread beyond the ovary, resulting in diagnosis at an advanced stage. As a result, there is a poor patient prognosis with only fifteen percent of women possessing advanced stage disease surviving for five years. Despite an initial clinical response of 80% to surgery and chemotherapy, most patients experience tumor recurrence within two years of treatment. The overwhelming majority of these patients will eventually develop chemoresistant disease and die.

Available for licensing are two gene signatures. One gene signature can predict whether a patient will initially respond to standard platinum-paclitaxel chemotherapy, but will relapse within six months of completing treatment. A second gene signature identifies patients who will show no response to therapy. This methodology may enable clinicians to identify patients who may be candidates for additional and/or novel chemotherapy drugs, and effectively choose appropriate cancer treatment. A unique feature of this signature is its derivation from pure, microdissected isolates of ovarian tumor cells, rather than undissected tissue. By utilizing this approach, the resulting gene list is specific to the cell type that causes the disease.

Applications: Method to detect if an ovarian cancer patient is sensitive to treatment with chemotherapeutic agents; Method to evaluate ovarian cancer patient chemoresponsiveness; Diagnostic tool to aid clinicians in determining appropriate cancer treatment; Methods to treat ovarian cancer identified by chemoresistant biomarkers compositions.

Market: Ovarian cancer is the fourth most common form of cancer in the U.S.; Ovarian cancer is three times more lethal than breast cancer; 15,310 deaths in the U.S. in 2006.

Development Status: The technology is currently in the pre-clinical stage of development.

Inventors: Michael J. Birrer (NCI) et al.

Publication: SC Mok et al. Biomarker discovery in epithelial ovarian cancer by genomic approaches. *Adv Cancer Res.* 2007;96:1-22.

Patent Status: U.S. Provisional Application No. 60/899,942 filed 06 Feb. 2007 (HHS Reference No. E-060-2007/0-US-01).

Licensing Status: Available for exclusive or non-exclusive licensing.

Licensing Contact: Jennifer Wong; 301/435-4633; wongje@mail.nih.gov.

Potent, Easy to Use Targeted Toxins as Anti-Tumor Agents

Description of Technology: The invention discloses synthesis and use of novel derivatives of 2-[2'-(2-aminoethyl)-2-methyl-ethyl]-1,2-dihydro-6-methoxy-3H-dibenz-[de,h]isoquinoline-1,3-dione as targeted anti-tumor agents. The use of targeted toxin conjugates with anti-cancer antibodies, such as herceptin, is increasing. Based on a comparison with the structurally complex toxins, such as DM1, available in the market, these novel toxins are more stable in circulation, thus making the toxin-conjugates more tumor-selective and

less toxic. As such, these compounds are superior alternatives to the existing toxins.

The invention describes a potent and easy to synthesize toxin that can be used for generating a variety of prodrugs. These compounds can be attached to a ligand that recognizes a receptor on cancer cells, or to a peptide that is cleaved by tumor-specific proteases. The compounds are topoisomerase inhibitors and are mechanistically different from DM1 that targets tubulin.

The structure of the toxin allows it to be modified with a peptide linker that is stable, but rapidly cleaved in lysosomes after the compound is specifically taken up by cancer cells.

Applications: The compounds can be used for preparation of a variety of potent anti-cancer agents with low systemic toxicity.

Advantages: Easy to prepare; Structural features make these compounds more stable in circulation; Toxin conjugates are more tumor-selective and less toxic.

Benefits: 600,000 cancer deaths occurred in 2006 in spite of advances in cancer therapeutics. A major limitation of current therapeutics is their toxic side effects. This technology can effectively treat cancer with low systemic toxicity and thus improve overall survival and quality of life of patients suffering from cancer. The current cancer chemotherapeutic market is valued at \$42 billion and expected to grow.

Inventors: Nadya I. Tarasova, Marcin D. Dyba, Christopher J. Michejda (NCI).

Development Status: *In vitro* studies are completed and *in vivo* animal model studies are ongoing.

Patent Status: U.S. Provisional Application No. 60/844,027 filed 12 Sep. 2006 (HHS Reference No. E-160-2006/0-US-01).

Licensing Contact: Mojdeh Bahar, J.D.; 301/435-2950; baharm@mail.nih.gov.

Dated: June 19, 2007.

Steven M. Ferguson,

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

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Heart, Lung, and Blood Institute; Amended Notice of Meeting

Notice is hereby given of a change in the meeting of the National Heart, Lung, and Blood Institute Special Emphasis