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*Patent Status:* U.S. Patent No. 6,562,347 issued 13 May 2003 (HHS Reference No. E-107-1998/0-US-03).

*Licensing Contact:* Patrick McCue, PhD; 301-435-5560; [mccuepat@mail.nih.gov](mailto:mccuepat@mail.nih.gov).

*Collaborative Research Opportunity:* The National Institute on Aging, Laboratory of Immunology, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize cancer vaccines that target skin antigen-presenting cells.

Please contact Nicole Guyton at 301-435-3101 or [guytonn@mail.nih.gov](mailto:guytonn@mail.nih.gov) for more information.

Dated: October 21, 2010.

**Richard U. Rodriguez,**  
*Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.*

[FR Doc. 2010-27179 Filed 10-26-10; 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, 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.

#### IL-10 and IFN $\gamma$ Peptide Inhibitors

*Description of Invention:* Available for licensing are several potent and selective inhibitors of IL-10 and IFN- $\gamma$  signaling. Although cytokines play important roles in cancer and inflammation, there are no specific inhibitors of any cytokines to date. IL-10 and IFN- $\gamma$  cytokine signaling play crucial roles in inflammation, cancer growth, and autoimmune diseases. The investigators have developed short peptides that potently and selectively interfere with dimerization of the cytokines and their binding to the corresponding receptor. Included in the patent application are also metabolically stable lipopeptides mimicking conserved regions of IL-10 and IFN- $\gamma$  receptors that interfere with STAT3 and

STAT1 phosphorylation and subsequent signaling. Lipopeptides potently inhibit STAT3 and STAT1-dependent growth of cancer cells. These compounds are promising drug candidates for the treatment of cancer and many infectious and inflammatory diseases.

*Application:* Cancer, viral infections and anti-inflammatory treatments.

*Advantages:*

- Potent, stable peptide inhibitors.
- Selective IL-10 and IFN- $\gamma$  inhibitors.

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

*Market:* The annual growth rate for the therapeutic peptide market is estimated at about 7.5%.

*Inventors:* Nadya Tarasova *et al.* (NCI).

*Patent Status:* U.S. Provisional Application No. 61/333,512 filed 11 May 2010 (HHS Reference No. E-167-2010/0-US-01).

*Licensing Status:* Available for licensing.

*Licensing Contact:* Jennifer Wong; 301-435-4633; [wongje@mail.nih.gov](mailto:wongje@mail.nih.gov).

*Collaborative Research Opportunity:* The Center for Cancer Research, Cancer and Inflammation Program, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize inhibitors of IL10, IFN $\gamma$  and STAT3 signaling. Please contact John Hewes, Ph.D. at 301-435-3121 or [hewesj@mail.nih.gov](mailto:hewesj@mail.nih.gov) for more information.

#### Diagnostic and Prognostic HCC-Related Metabolites

*Description of Invention:* Metabolite profiling identifies and measures changes in cellular metabolites as a means to determine a direct correlation between gene expression and changes in biological function. Investigators at the National Cancer Institute have identified a unique set of metabolite biomarkers associated with hepatocellular carcinoma (HCC), early stage HCC, HCC patient outcome and HCC stem-cell subtype. Subsets of this metabolite/gene signature can distinguish HCC tumors from normal tissues with 88–97% accuracy, identify early stage HCC patients with 62–78% accuracy, wherein early stage is defined as TNM stage I, prognose negative patient outcome, and identify a HCC stem cell subtype with 70–77% accuracy. These metabolites and gene surrogates are elements of the PI3K and Myc signaling networks which can potentially be targeted for therapeutic purposes.

HCC represents an extremely poor prognostic cancer, and patients are often diagnosed with end-stage cancer and have poor survival. HCC is also a very heterogeneous disease and often arises from chronic liver disease. Surgery and transplantation remain the only curative option for patients; however, complications due to cirrhosis mean it is a viable option for 5–10% patients. This HCC gene signature can be developed into assays to enable clinicians to accurately diagnose HCC, including early stages and subtype of this disease, and therefore stratify patients for appropriate treatment and prioritizing liver transplantation candidates based on their metabolite profile.

*Applications:*

- Method to diagnose HCC, including HCC subtypes.

- Method to prognose HCC patient outcome.

- Method to stratify patients for appropriate treatment.

*Advantages:* Highly accurate metabolite/gene profile that can be developed into a variety of diagnostic and prognostic applications.

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

*Market:*

- Global oncology biomarker discovery market is expected to grow from \$2.5 billion in 2009 to \$5.7 billion by 2014.

- North America has the largest metabolomic market with an estimated value of \$161.4 million in 2009, and it is projected to reach \$324 million by 2014.

- HCC is the fifth most common cancer worldwide with an estimated one million new cases diagnosed annually.

*Inventors:* Xin Wei Wang and Anuradha S. Budhu (NCI).

*Patent Status:* U.S. Provisional Application No. 61/323,420 filed 13 Apr 2010 (HHS Reference No. E-139-2010/0-US-01).

*Licensing Status:* Available for licensing.

*Licensing Contact:* Jennifer Wong; 301-435-4633; [wongje@mail.nih.gov](mailto:wongje@mail.nih.gov).

*Collaborative Research Opportunity:* The Center for Cancer Research, Laboratory of Human Carcinogenesis, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize metabolomic signatures for liver cancer. Please contact John Hewes, Ph.D. at 301-435-3121 or [hewesj@mail.nih.gov](mailto:hewesj@mail.nih.gov) for more information.

### Stimulation of Natural Killer T-Cell Anti-Tumor Activity

*Description of Invention:* Natural killer T cells (NKT) are a unique lymphocyte population that has T-cell and NK cell functional properties in order to rapidly elicit an immune response.  $\alpha$ -galactosylceramide ( $\alpha$ -GalCer) is a potent NKT stimulator and induces of IFN- $\gamma$  release to promote immunity against tumors and infectious agents. Humans have natural antibodies against  $\alpha$ -galactose, which may be one of the reasons why the human clinical trials of  $\alpha$ -GalCer or KRN7000 were not very successful.

Investigators at the National Cancer Institute have found that  $\beta$ -mannosylceramide ( $\beta$ -ManCer) promotes immunity in an IFN- $\gamma$  independent mechanism.  $\beta$ -ManCer is a new class of NKT agonist that induces immune responses alone, through nitric oxide and TNF- $\alpha$ -dependent mechanisms, or synergistically with  $\alpha$ -GalCer to enhance  $\alpha$ -GalCer's efficacy. Since  $\beta$ -ManCer does not have  $\alpha$ -galactose, which can be neutralized by natural antibodies, patients could be treated with multiple doses without negative side effects associated with the loss of IFN- $\gamma$  production. Hence,  $\beta$ -ManCer is a promising anti-cancer treatment either alone or in combinatorial therapies with  $\alpha$ -GalCer to selectively induce immune responses.

*Applications:*

- Cancer therapeutics.
- Potent stimulator of NKT activity.

*Advantages:*

- Induces tumor immunity through a novel mechanism.

- Decreased possibility of neutralization by natural antibodies.

- Synergize with  $\alpha$ -GalCer.

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

*Market:* Global cancer market is worth more than eight percent of total global pharmaceutical sales.

*Inventors:* Masaki Terabe (NCI) *et al.*

*Patent Status:* U.S. Provisional Application No. 61/313,508 filed 12 Mar 2010 (HHS Reference No. E-034-2010/0-US-01).

*Licensing Status:* Available for licensing.

*Licensing Contact:* Jennifer Wong; 301-435-4633; [wongje@mail.nih.gov](mailto:wongje@mail.nih.gov).

*Collaborative Research Opportunity:* The Vaccine Branch of the National Cancer Institute is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize  $\beta$ -ManCer. Please contact John Hewes, Ph.D. at 301-435-3121 or

[hewesj@mail.nih.gov](mailto:hewesj@mail.nih.gov) for more information.

### Modified POTE Peptides for Cancer Immunotherapy

*Description of Invention:* Investigators at the National Cancer Institute have identified and enhanced immunogenicity of POTE epitopes to improve their efficacy in cancer vaccines. POTE is a novel tumor antigen expressed in a variety of cancers including breast, prostate, colon, lung, ovary, and pancreas cancers. POTE has limited expression in normal tissues and therefore a specific target for cancer treatments, including immunotherapy. Immunotherapy has great potential as a cancer therapeutic because of its specificity and freedom from toxic effects of chemotherapies.

Antigen-specific cancer immunotherapy often relies on identification of epitopes expressed by cancer cells that can be targeted by cytotoxic T cells (CTL). However, the CTL repertoire against high-affinity cancer epitopes is often ineffective because cancer epitopes may share a similar structure to natural "self" antigens. As a result, cancer cells are not recognized by CTLs and destroyed. The enhanced POTE epitopes induce a stronger immune response than natural responses. These modified epitopes are more effective at inducing CTL against POTE expressing cancer cells and have greater potential to serve as cancer vaccine targets.

*Applications:*

- Therapeutic cancer vaccine.
- Method to treat cancer.

*Advantages:*

- Enhanced immunogenic peptides.
- Cancer vaccines that overcome self-tolerance to target a variety of tumor cells.

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

*Market:* The therapeutic cancer market will be worth an estimated \$633 million in 2014.

*Inventors:* Jay A. Berzofsky, Yi-Hisang Huang, Ira Pastan, Masaki Terabe (NCI).

*Patent Status:* U.S. Provisional Application No. 61/313,559 filed 12 Mar 2010 (HHS Reference No. E-003-2010/0-US-01).

*Licensing Status:* Available for licensing.

*Licensing Contact:* Jennifer Wong; 301-435-4633; [wongje@mail.nih.gov](mailto:wongje@mail.nih.gov).

*Collaborative Research Opportunity:* The Center for Cancer Research, Vaccine Branch, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or

commercialize this technology. Please contact John Hewes, Ph.D. at 301-435-3121 or [hewesj@mail.nih.gov](mailto:hewesj@mail.nih.gov) for more information.

Dated: October 21, 2010.

**Richard U. Rodriguez,**

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

[FR Doc. 2010-27181 Filed 10-26-10; 8:45 am]

BILLING CODE 4140-01-P

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#### Photosensitizing Antibody-Fluorophore Conjugate for Photo-Immunotherapy

*Description of Invention:* A major goal of targeted cancer therapy is to improve the sensitivity and specificity of the therapy so that cancer cells can be detected and targeted for elimination, while normal cells in the surrounding area remain largely intact. Photodynamic therapy (PDT) is a treatment for cancer and non-cancerous lesions involving light and a photosensitizer. The photosensitizer can be targeted to a specific cell using antibodies specific for proteins expressed on the target cell surface, the target cells will then be destroyed after being exposed to light at appropriate wavelength.

The NIH technology describes a method of photosensitizing cancerous cells by irradiating an antibody fluorophore conjugate. The NIH investigators have conducted in vitro studies using a proprietary IRDye 700DX NHS Ester. The IR700 dye was conjugated to a proprietary humanized anti-HER1 or anti-HER2 or anti-PSMA antibody, Panitumumab or Trastuzumab or huJ591. Subsequent irradiation of non-ionizing near infrared light showed rapid cell death of tumor cells, while normal cells were not noticeably killed. The studies were repeated in mice with similar results.

#### *Applications and Market:*

- Photodynamic therapy for cancer by selective targeting and killing of cells without suffering normal tissue side effects.

- Cancer was responsible for about 13% of all human deaths in 2007. There remains a need for therapies that effectively kill the tumor cells while not harming non-cancerous cells.

*Development Status:* Both *in vitro* and *in vivo* data available.

*Inventors:* Hisataka Kobayashi, Peter L. Choyke, Makoto Mitsunaga (NCI)

*Publications:* Manuscript in submission.

*Patent Status:* U.S. Provisional Patent Application No. 61/363,079, filed July 9, 2010 (HHS Reference No. E-205-2010/0-US-01)

*Licensing Status:* Available for licensing.

*Licensing Contact:* Betty B. Tong, PhD; 301-594-6565; [tongb@mail.nih.gov](mailto:tongb@mail.nih.gov).

#### Soluble Glypican-3 Protein for Treatment of Cancer

#### *Description of Technology:*

Hepatocellular carcinoma (HCC) is a form of liver cancer that is among the more deadly cancers in the world. HCC is typically only detected at the later stages of cancer development, which is always associated with poor prognosis. Because HCC is often associated with liver disease, traditional chemotherapy is not an option, making surgery the most common form of treatment. As a result, there is a need for new treatments.

Glypican-3 (GPC3) is a cell surface protein that is normally involved in cell growth and differentiation. GPC3 has been shown to act through the Wnt-signaling pathway, a pathway that is often activated in a number of different cancer cell types. Significantly, the ability of GPC3 to activate signaling through Wnt requires that GPC3 be bound to the cell membrane. GPC3 is also preferentially expressed on HCC cells, suggesting it could play a

particularly important role in tumorigenesis in HCC.

This invention concerns a soluble form of GPC3 that lacks its cell membrane anchoring domain. This soluble form of GPC3 maintains its ability to interact with the Wnt signaling pathway, but cannot induce the activation of the pathway because it is not bound to the cell membrane. By competing with fully functional GPC3, the soluble GPC3 is able to inhibit the growth of HCC cells, thereby decreasing the ability of tumors to grow and metastasize. This suggests that soluble GPC3 represents a possible therapeutic for HCC.

#### *Applications:*

- Soluble GPC3 represents a potential therapeutic for patients with cancer with hyperactivated Wnt-signaling pathways.

- Specific cancers include hepatocellular cancer (HCC), melanoma, thyroid cancer, lung squamous cell carcinoma, Wilms' tumor, neuroblastoma, hepatoblastoma, and testicular germ-cell tumors.

#### *Advantages:*

- Removal of the glycosyl-phosphatidylinositol (GPI) anchor results in a soluble form of GPC3 that can interrupt Wnt-signaling.
- Soluble GPC3 maintains the ability to compete with fully functional GPC3 despite its inability to activate signaling.
- For treatment of HCC, offers a non-invasive, potentially non-liver toxic alternative to current strategies.

*Development Status:* Preclinical stage of development; cell culture data with HCC cells

*Inventors:* Ho (NCI) *et al.*

*For more information, see:*

- "Recombinant soluble glypican 3 protein inhibits the growth of hepatocellular carcinoma in vitro" Feng *et al.* Int. J. Cancer: E-pub (8 July 2010).

- "Soluble Glypican 3 inhibits the growth of Hepatocellular Carcinoma in vitro and in vivo" Zitterman *et al.* Int. J. Cancer: 126, 1291-1301 (2010).

*Patent Status:* U.S. provisional applications 61/334,135 (E-176-2010/0-US-01) and 61/350,722 (E-176-2010/1-US-01).

*Licensing Status:* Available for licensing.

*Licensing Contact:* David A. Lambertson, PhD; 301-435-4632; [lambertsond@mail.nih.gov](mailto:lambertsond@mail.nih.gov).

*Collaborative Research Opportunity:* The National Cancer Institute, Laboratory of Molecular Biology, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology. Please contact John Hewes,