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.

BODIPY®-FL Nilotinib (Tasigna®) for Use in Cancer Research

Description of Invention: Investigators at the National Institutes of Health have produced a fluorescently labeled derivative of the clinically-approved, tyrosine kinase inhibitor (TKI) nilotinib (Tasigna®) for use in research. This was accomplished by conjugating the fluorescent dye BODIPY®-FL to nilotinib.

The TKI imatinib (Gleevec®) is the first targeted therapeutic developed and is used as first line treatment of Philadelphia chromosome-positive (Ph+) cancers like chronic myeloid leukemia (CML). Although imatinib is highly effective, after continued use the cancer cells frequently become resistant to the drug. Nilotinib is a second generation TKI developed to overcome imatinib resistance, but eventually it can also result in drug resistance.

The fluorescent nilotinib conjugate was developed to study the mechanism by which cancer cells become resistant to nilotinib and better understand its cytotoxic effects.

Applications

- Use in monitoring cellular accumulation of nilotinib using flow cytometry, fluorescent microscopy, or other fluorometric techniques
- Use as an *in vivo* probe with experimental models and in clinical studies for analyzing drug efficacy, pharmacokinetic profile and drug localization
- Use for the study of cytotoxic effects of nilotinib in important physiological locations such as the heart and brain
- Use in identifying other potential targets of nilotinib in different types of cancer
- Use in *in vivo* imaging to identify potential physiological barriers to drug penetration into tissues

Advantages

- Material is ready for use reducing time and effort to duplicate
- BODIPY®-FL dye is compatible with commonly-used fluorescein dye optics and has superior can be used for both *in vitro* and *in vivo* studies.

Development Status:

- Ready for use.
- Pre-clinical data available.

Market: The size of the chronic myeloid leukemia (CML) market is expected fluorescent properties to fluorescein

- BODIPY®-FL Nilotinib (Tasigna®) is compatible and to increase with an aging population. It was estimated that in 2009, there were 91,500 patients with CML in the U.S. and other major other developed countries, increasing by 9–11% per year. The fluorescently- labeled Nilotinib (Tasigna®) will be useful for researchers working to develop next generation tyrosine kinase inhibitors.

Inventors: Suneet Shukla (NCI), Suresh V. Ambudkar (NCI), Craig J. Thomas (NHGRI/NCGC), Amanda P. Skoumbourdis (NHGRI/NCGC).

Publications: None currently available for this technology.

Patent Status: HHS Reference No. E–009–2010/0—Research Tool. Patent protection is not being pursued for this technology.

Licensing Status: Available for biological materials licensing.

Licensing Contact: Sabarni Chatterjee, Ph.D.; 301–435–5587; *chatterjeesa@mail.nih.gov.*

Collaborative Research Opportunity: The National Cancer Institute, Transport Biochemistry Section, Laboratory of Cell Biology, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize bodipy conjugated tyrosine kinase inhibitors that are currently used in the clinic for the treatment of CML or gastric cancers. We are also interested in evaluating third generation tyrosine kinase inhibitor derivatives as modulators of ABC drug transporters to improve the efficiency of chemotherapy in animal (mouse) model system. In addition, we can identify possible pharmacokinetic interactions of the novel kinase inhibitors with ABC drug transporters. Please contact John Hewes, Ph.D. at 301–435–3131 or *hewesj@mail.nih.gov* for more information.

Diagnosis and Treatment of Cancer Using Histone Deacetylase Inhibitors and Radiolabeled Metaiodobenzylguanidine

Description of Invention: Pheochromocytoma is a neuroendocrine tumor of the adrenal glands. Pheochromocytoma patients display the signs and symptoms of those of sympathetic nervous system hyperactivity. Up to 36% of patients worldwide with pheochromocytoma develop metastatic disease and have a 5-year survival rate of approximately 50% after diagnosis. Patients with metastatic pheochromocytoma exhibit excessive levels of circulating catecholamines, which results in increased risk of strokes, cardiac arrhythmias, and hypertensive complications. Current treatments for malignant pheochromocytoma include targeted radiation using [^{131}I]-metaiodobenzylguanidine ([^{131}I]-MIBG), cytotoxic chemotherapy, octreotide, tumor hemoembolization, etc. The success of these treatments varies based on the sites and growth rate of metastatic lesions.

The present invention provides a method for treating a mammalian tumor with a histone deacetylase inhibitor (HDACi), and followed by administering [^{131}I]-MIBG. Methods of diagnosis and imaging of mammalian tumors are also disclosed. These findings suggest that HDACi could enhance the therapeutic efficacy of [^{131}I]-MIBG treatment in patients with malignant pheochromocytoma.

Applications and Market:

- Diagnosis and therapeutic for treating cancer, such as pheochromocytoma.
- Approximately 1000 cases of pheochromocytoma are diagnosed in United States yearly.

Development Status: Pre-clinical stage of development.

Inventors: Karel Pacak et al. (NICHD).

Publications: Manuscript submitted.

Patent Status: U.S. Provisional Application No. 61/260,991 filed 13 Nov 2009 (HHS Reference No. E–299–2009/0–US–01).

Licensing Status: Available for licensing.

Licensing Contact: Betty B. Tong, PhD; 301–594–6565; *tongb@mail.nih.gov.*

Collaborative Research Opportunity: The National Institute of Child Health and Human Development, Reproductive Biology and Adult Endocrinology Branch, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize [^{131}I]-MIBG treatment of malignant/metastatic pheochromocytoma, paraganglioma, and neuroblastoma; also [$^{123/131}$I]-MIBG scintigraphy—in all situations histone deacetylase to be used before MIBG is used. Please contact Joseph Conrad, PhD at 301–435–3107 or *jmconrad@mail.nih.gov* for more information.

Specific Binding Agents for KSHV vIL–6 That Neutralize a Biological Activity

Description of Invention: Kaposi's sarcoma-associated herpes virus (KSHV) is an oncogenic herpes virus originally identified in AIDS associated Kaposi's sarcoma (KS) lesions, the most common tumor associated with HIV infection. KSHV encodes various proteins that have characteristics associated with cellular growth and transformation, including viral (v) IL–6 (KSHV vIL–6). These viral proteins display structural homology to their cellular counterparts, and human and vIL–6 are multifunctional cytokines that have been shown to induce vascular endothelial growth factor and other factors.

Available for licensing are binding agents that neutralize vIL–6 biological activities, methods of diagnosing and treating KSHV disorders, and methods to monitor KSHV patient response to treatment. Deregulation of cellular IL–6 expression is known to contribute to tumor development, suggesting that KSHV-derived vIL–6 could be part of a viral strategy to promote malignant transformation. Neutralizing activity of anti-vIL–6 antibodies may provide a potential therapeutic for KSHV disorders such as HIV, Castleman's disease, and primary effusion lymphoma.

Applications:

- Therapeutic compositions to treat KSHV disorders such as KS, Castleman's disease, and primary effusion lymphoma.
- Method to diagnose and treat KSHV disorders.
- Method to monitor patient response to KSHV treatment.

Market:

- Approximately 476,095 persons currently living with HIV/AIDS in the United States.
- Estimated annual incidence rate for KS is 5 cases per 100,000/year in the U.S.
- KS contributes to approximately 30% of AIDS related deaths.

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

Inventors: Giovanna Tosato (NCI) et al.

Publications:

1. Y Aoki and G Tosato. Therapeutic options for human herpesvirus-8/ Kaposi's sarcoma-associated herpesvirus-related disorders. Expert Rev Anti Ther. 2004 Apr;2(2):213–225. [PubMed: 15482187].

2. Y Aoki et al. Detection of viral interleukin-6 in Kaposi sarcoma-associated herpesvirus-linked disorders. Blood. 2001 Apr 1;97(7):2173–2176. [PubMed: 11264189].

3. Y Aoki et al. Kaposi's sarcoma-associated herpesvirus-encoded interleukin-6. J Hemathother Stem Cell Res. 2000;9(2):137–145. [PubMed: 10813527].

Patent Status:

U.S. Patent No. 6,939,547 issued 06 Sep 2005 (HHS Reference No. E–180–2000/0–US–03).

U.S. Patent No. 7,108,981 issued 19 Sep 2006 (HHS Reference No. E–180–2000/0–US–04).

U.S. Patent No. 7,235,365 issued 26 Jun 2007 (HHS Reference No. E–180–2000/0–US–05).

U.S. Patent No. 7,374,756 issued 20 May 2008 (HHS Reference No. E–180–2000/0–US–06).

Licensing Status: Available for licensing.

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

Collaborative Research Opportunity: The National Cancer Institute's Laboratory of Cellular Oncology is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize therapeutics for Kaposi's sarcoma-associated herpes virus (KSHV). Please contact John D. Hewes, PhD at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Dated: March 1, 2010.

Richard U. Rodriguez,

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

[FR Doc. 2010–4762 Filed 3–4–10; 8:45 am]

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Patient-Derived Gastrointestinal Stromal and Paraganglioma Tumor Samples Harboring Novel Stem Cell Factor *FOXD3* Variants

Description of Invention: The cancer market is forecast to reach $40 billion dollars by the year 2012. There is still a significant need to develop new therapies for treating sarcomas and malignant neoplasms.

Researchers at the National Institute of Child Health and Human Development (NICHD), NIH, have made available samples of patient-derived gastrointestinal tumors (GIST) and paraganglioma tumors that harbor genetic mutations that have an effect on early stage embrogenesis which plays a role in the fate of stem cells. GISTs are one of the most common sarcomas of the gastrointestinal tract with an estimated 5,000–10,000 new cases in the U.S. reported each year. GISTs affect mainly pediatric and young adult patients, and respond poorly to current therapies. Paragangliomas are rare neuroendocrine neoplasms that develop primarily in the abdomen.

The tumor samples made available herein contain deletions in the *FOXD3* gene and display down-regulated FOXD3 protein expression. While the