

*Licensing Contact:* Betty B. Tong, PhD; 301-594-6565; [tongb@mail.nih.gov](mailto: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 [<sup>131</sup>I]-MIBG treatment of malignant/metastatic pheochromocytoma, paraganglioma, and neuroblastoma; also [<sup>123/131</sup>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](mailto: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 Hematother 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](mailto: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](mailto: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]

**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.

#### **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 embryogenesis 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

majority of GISTs result from activating mutations in the oncogene receptor tyrosine kinases *c-KIT* and *PDGFRA*, these tumor samples do not harbor mutations in *c-KIT* or *PDGFRA* ("non-*KIT*/*PDGFRA*-GISTs") and respond poorly to receptor tyrosine kinase inhibitors.

**Applications:**

- Useful in the investigation of inactivating genetic changes in *FOXD3* in non-*KIT*/*PDGFRA*-GISTs.

- Useful in the study of new molecules and/or pathways that may serve as an appropriate therapeutic target.

**Inventors:** Constantine Stratakis et al. (NICHD).

**Patent Status:** HHS Reference No. E-058-2010/0—Research Tool. Patent protection is not being pursued for this technology.

**Licensing Status:** Available for licensing under a biological material license.

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

**Collaborative Research Opportunity:** The National Institute of Child Health and Human Development Endocrinology & Genetics Section is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology. Please contact Joseph Conrad, PhD at 301-435-3107 or [jmconrad@mail.nih.gov](mailto:jmconrad@mail.nih.gov) for more information.

### Novel Kinase Inhibitors Targeting the PH Domain of AKT for Preventing and Treating Cancer

**Description of Invention:** Activation of the PI3K/Akt signaling pathway has been implicated in the development of cancer. Akt, a kinase that is central to this pathway, is found at elevated levels in many tumors and is associated with a poor disease prognosis. Many research studies have validated Akt as a therapeutic target for the development of anti-cancer drugs. Most efforts of drug development targeting Akt have focused on inhibitors of the ATP-binding domain which tend to interfere with other physiologically important kinases. An alternative strategy that has been proposed to improve drug specificity is the targeting of the unique pleckstrin homology (PH) domain of Akt.

Investigators at the National Institutes of Health have screened a library of small chemical compounds with drug-like characteristics that likely bound to the PH domain and have identified several candidates previously unknown to interact with Akt. These compounds

were tested and found to inhibit Akt activity specifically through the PH domain. Some of these compounds demonstrated broad cytotoxicity to a wide variety of tumor cells. These novel Akt-inhibiting compositions target the PH domain and help in the prevention and treatment of cancer. Since it has been shown that reducing the activity of the PI3K-Akt pathway sensitizes malignant cells to chemotherapy or radiotherapy, these novel Akt inhibitors have potential either as single anti-cancer agents or in combination with conventional cancer therapies.

One of the candidate compounds inhibited Colony Stimulating Factor-1 Receptor (CSF1R) from binding to ATP but had no activity for other kinases. CSF1R has been implicated in development of cancers like chronic myelomonocytic leukemia, but also in Alzheimer's disease so this specific compound may have use in treating other diseases in addition to cancer.

**Applications:**

- Treating or preventing development of cancer or preventing progression of premalignant lesions to cancer.

- Used as a single agent or in combination with other anti-cancer treatments like chemotherapy, biological therapy, or radiation.

- Inhibiting the activity of CSF1R receptor to treat diseases like chronic myelomonocytic leukemia and Alzheimer's disease or an adverse condition, such as brain injury.

**Advantages:** Targeting the PH domain improves specificity against Akt kinase in comparison to inhibitors of the ATP domain which typically are unspecific.

**Inventors:** Phillip A. Dennis (NCI) et al.

**Patent Status:** U.S. Provisional Application No. 61/226,328 filed 17 Jul 2009 (HHS Reference No. E-212-2009/0-US-01).

**Licensing Status:** Available for licensing.

**Licensing Contact:** Surekha Vathyam, PhD; 301-435-4076; [vathyams@mail.nih.gov](mailto:vathyams@mail.nih.gov).

**Collaborative Research Opportunity:** The Center for Cancer Research, Medical Oncology Branch and Affiliates, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology. Please contact John D. Hewes, PhD at 301-435-3121 or [hewesj@mail.nih.gov](mailto:hewesj@mail.nih.gov) for more information.

### Diagnostic Biomarker of Metastasis for Improved Clinical Management of Head and Neck Cancer

**Description of Invention:** Squamous Cell Carcinoma of the Head and Neck (HNSCC) is associated with poor prognosis due to the advanced stage of disease (metastasis) typically found at the time of diagnosis. Investigators at the NIH have developed a sensitive method using a protein biomarker for detecting even just a few HNSCC tumor cells in lymph nodes with occult disease. Combination of this staging technique with intraoperative sentinel lymph node mapping would improve the management of HNSCC by identifying patients for which radical lymph node dissection is most appropriate, sparing those for which it is not, and informing decisions for adjuvant cancer therapy during a single surgery.

This technology arose from the discovery that the Desmoglein-3 (DSG3) protein which is highly expressed in tumors of squamous epithelial origin, like HNSCC, is also expressed in invaded lymph nodes but it is not found in normal lymph nodes. Therefore, DSG3 can serve as a biomarker for detecting metastatic spread of squamous cell carcinoma tumors. This is achieved by performing protein detection immunoassays to samples (biopsy, aspirate, or isolated cells) of suspect lymph nodes.

**Applications:** Use with sentinel lymph node mapping for rapid, intraoperative diagnosis of metastatic HNSCC for guiding proper therapeutic approach.

**Advantages:**

- Rapid diagnosis during surgery increases effectiveness of intervention thereby reducing need for subsequent surgery.

- Improved accuracy of direct measurement of protein levels over RNA assays.

- More robust assay as protein is more stable than RNA.

**Development Status:**

- Early stage.
- Clinical data available.

**Market:** HNSCC is the sixth most prevalent cancer among men worldwide and is associated with poor prognosis, which has improved only marginally over the past three decades. This is reflected by HNSCC being the eighth leading cause of cancer death worldwide.

**Inventors:** J. Silvio Gutkind et al. (NIDCR).

**Related Publication:** Patel V, Hood BL, Molinolo AA, Lee NH, Conrads TP, Braisted JC, Krizman DB, Veenstra TD,

Gutkind JS. Proteomic analysis of laser-captured paraffin-embedded tissues: a molecular portrait of head and neck cancer progression. Clin Cancer Res. 2008 Feb 15;14(4):1002–1014. [PubMed: 18281532].

**Patent Status:** U.S. Provisional Application No. 61/186,582 filed June 6, 2009 (HHS Reference No. E-300-2008/0-US-01).

**Licensing Status:** Available for licensing.

**Licensing Contact:** Whitney Hastings, PhD; 301-451-7337; [hastingsw@mail.nih.gov](mailto:hastingsw@mail.nih.gov).

**Collaborative Research Opportunity:** The NIDCR, OPCB, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize the use of DSG3 as a biomarker for detecting metastatic spread of squamous cell carcinoma tumors. Please contact David W. Bradley, PhD at [bradleyda@nidcr.nih.gov](mailto:bradleyda@nidcr.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. 2010-4761 Filed 3-4-10; 8:45 am]

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Confidential Disclosure Agreement will be required to receive copies of the patent applications.

#### Long Acting Ophthalmic Analgesic Eye Drops

**Description of Invention:** This invention is directed to the discovery that resiniferatoxin (RTX) produces a three to four day analgesic effect when topically applied to the cornea. Efficacy for RTX as an effective analgesic has been demonstrated in vivo in rats. Importantly, unlike currently available analgesics, RTX left the blink reflex intact and did not impact mechanical sensitivity. RTX also did not impair epithelial wound healing and functioned without detectable damage to the cornea.

RTX is a potent agonist of the transient receptor potential channel, subfamily V, member 1 (TRPV1). TRPV1 is involved in pain sensation and is expressed only in select neurons. Unlike other local analgesics that target a wide breadth of neurons, RTX targets only those neurons that express TRPV1, leaving the important blink reflex and mechanical sensitivity of the eye unaffected.

##### Applications:

- An ophthalmic analgesic for post-operative eye pain.
- An ophthalmic analgesic for acute or chronic eye injury.
- Applicable to both human and veterinary patients.

##### Advantages:

- Both long lasting and reversible.
- Does not impair epithelial wound healing, leaves the blink reflex intact, and functions without detectable damage to the cornea.

##### Development Status:

- Early stage.
- Demonstrated efficacy *in vivo* in rats.

**Market:** Twenty-six million people worldwide experience neuropathic pain, resulting in healthcare costs of over three billion dollars per year.

**Inventors:** Michael J. Iadarola, Andrew J. Mannes, Jason M. Keller, Kendall Mitchell, Brian D. Bates (NIDCR).

**Publication:** In preparation.

**Patent Status:** U.S. Provisional Application No. 61/247,881 filed 01 Oct 2009 (HHS Reference No. E-117-2009/0-US-01).

**Licensing Status:** Available for licensing.

**Licensing Contact:** Charlene Sydnor, PhD; 301-435-4689; [sydnorc@mail.nih.gov](mailto:sydnorc@mail.nih.gov).

**Collaborative Research Opportunity:** The National Institute of Dental and Craniofacial Research, Laboratory of

Sensory Biology, Neurobiology and Pain Therapeutics Section, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology. Please contact David W. Bradley, PhD at 301-402-0540 or [bradleyda@nidcr.nih.gov](mailto:bradleyda@nidcr.nih.gov) for more information.

#### Novel Compositions for Use as Bone Scaffolds and Enhancers of Bone Regeneration

**Description of Invention:** This invention is directed to the discovery that a mixture of an organic polymer and inorganic particles may hold therapeutic utility as a biomaterial for artificial bone scaffolds, injectable bone-filling materials, and enhancement of new bone generation. This composition has demonstrated utility in vivo in mice.

The inventors have discovered a means of producing a stably homogenous mixture of the organic polymer and inorganic particles by crosslinking the two components. In contrast to current technologies, this invention not only imparts sufficient mechanical and load-bearing strength but also provides a suitable environment for new bone formation. Importantly, since the chemical reaction applied to make this biomaterial does not produce any harmful molecules or heat, it can be used in an injectable form. Bone formation or replacement is often a desired therapy for bone loss or defects due to fractures or bone degenerative diseases.

##### Applications:

- Injectable bone-filling materials.
- Artificial bone sponge for bone defect.
- Artificial bone sponge for bone cell culture in bone and mineralization research.

##### Advantages:

- Combines bone-like strength and a suitable environment for new bone formation

- Injectable.

##### Development Status:

- Early stage.
- Tested *in vivo* in mice.

**Market:** According to Freedoniagroup.com, the US orthopedic implant market was \$14.3 billion in 2007 and is expected to grow 8.9 percent annually through 2012. (<http://www.freedoniagroup.com/Orthopedic-Implants.html>, accessed December 2, 2009.)

**Inventors:** EunAh Lee and Pamela Robey (NIDCR) et al.

**Publication:** In preparation.

**Patent Status:**