the docket number found in brackets in the heading of this document.

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Dated: February 14, 2011.

Jane A. Axelrad,

Associate Director for Policy, Center for Drug Evaluation and Research.

[FR Doc. 2011–6509 Filed 3–18–11; 8:45 am]

BILLING CODE 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.

UOK 268 Cell Line for Hereditary Leiomyomatosis and Renal Cell Carcinoma

Description of Technology: Hereditary Leiomyomatosis and Renal Cell Carcinoma (HLRCC) is an extremely aggressive cancer syndrome with no effective treatment regimen and currently no cure. The progress of identifying HLRCC treatments and cures has likely been hindered due to the lack of an HLRCC model for studying the cancer syndrome and for screening therapeutic drug candidates.

This technology describes the UOK 268 cell line, a spontaneously immortalized renal tumor cell line that may be of great interest to industry for studying HLRCC, drug screening, and searching for tumor markers related to diagnosis, prognosis, and drug resistance. This cell line is only the second spontaneously immortalized cancer cell line of its kind in the world and is unique in that it is a primary tumor cell model (the other cell line, UOK 262, is from a metastasis cell model). The UOK 268 cell line is an established, clonal, immortalized renal cancer cell line derived from the long-term culture of aggressive tumor tissues of HLRCC in a specially designed culture medium under strict culture conditions. The UOK 268 exhibits an array of HLRCC kidney cancer characteristics that can promote protein and fatty acid biosynthesis and modulate HIF activities in a manner conducive to cancer cell proliferation.

Benefits:

• This is only one of two immortalized HLRCC cell lines, and is unique in that it is from a primary tumor cell model.

• Developing a diagnostic to search for tumor targets and screen for HLRCC and related cancers drug candidates will have significant benefits, including early detection and treatment.

Applications:

• *In vitro* and *in vivo* cell model for understanding the biology of HLRCC and related cancers, including growth, motility, invasion, and metabolite production.

• High throughput screening to test for drug candidates that could be used to treat particular cancers, such as HLRCC.

• Diagnostic tool for the diagnosis, prognosis, and drug resistance of tumor markers.

Advantages:

• *Cell line is derived from a HLRCC patient:* This cell line is anticipated to retain many features of primary HLRCC samples and novel HLRCC antigens identified from this cell line are likely to correlate with antigens expressed on human HLRCC tumors. Studies performed using this cell lines may have a direct correlation to the initiation, progression, treatment, and prevention of HLRCC in humans.

• *Molecular and genetic features are well characterized:* The inventors have elucidated many physical characteristics of the cell lines and their data reveals previously unrecognized coordination between mammalian glucose and iron metabolisms through AMPK signaling, and a novel mechanism for modulating HIF activities in renal cancers.

Inventors: W. Marston Linehan and Youfeng Yang (NCI)

Publications:

1. Youfeng Yang et al. Distinct Mito-transcriptome Profiling in Fumarate Hydratase-deficient Novel Primary Tumor Cell Line UOK268 Leads to Better Understanding of Early Human HLRCC-associated Cancer with Multiple Dysregulated Molecular Events and Metabolic Shunts. *Under submission.*

2. Wing-Hang Tong et al. Hypoactivation of AMPK pathway and remodeling of iron metabolism in hereditary leiomyomatosis and renal cell carcinoma tumorigenesis. *Under resubmission.*

Patent Status: HHS Reference No. E–254–2010/0—Research Tool. Patent protection is not being pursued for this technology.

Licensing Status: Available for licensing.

Licensing Contact: Whitney Hastings; 301–451–7337; *hastingw@mail.nih.gov.*

Collaborative Research Opportunity: The Center for Cancer Research, Urologic Oncology Branch, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize UOK268 as human HLRCC primary cell line model to comparing previously established UOK262, which was from metastasis lympho node. UOK 268 is a unique cell model for studying the underlying molecular derangements associated with impaired oxidative phosphorylation in cancer and for evaluating novel therapeutic approaches for this HLRCC-associated kidney cancer. Please contact John Hewes, PhD at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Agonistic Human Monoclonal Antibodies Against DR4

Description of Technology: The tumor necrosis factor (TNF)-related apoptosis-inducing ligand (TRAIL) and its functional receptors, DR4 and DR5, have been recognized as promising targets for cancer treatment. Therapeutics targeting TRAIL and its receptors are not only effective in killing many types of tumors but they also synergize with traditional therapies, and show efficacy against tumors that are otherwise resistant to conventional treatments.

The researchers at the NIH have developed two human monoclonal antibodies (mAbs) that bind to death receptor 4 (“DR4”). One of the mAbs is agonistic and inhibits the growth of ST486 cells with IC50 of about 10nM. The two mAbs were selected from a human phage-displayed Fab library by panning against a recombinant DR4

extracellular domain. Therefore the two mAbs are fully human. These antibodies could have considerable potential as cancer therapeutics alone or in combination with other drugs. Further, these antibodies could be used as a research tool for the study of DR4.

Applications:

• The DR4 antibodies could be promising candidate cancer therapeutics. Ongoing phase I and II clinical trials with mostly DR5-targeting agonistic antibodies have indicated that they are safe and could be efficacious for certain indications.

• DR4 is expressed in a broad range of solid tumors and malignancies and therefore antibodies to DR4 would be also useful reagents to study this expression.

Development Status: Pre-clinical proof of principle

Inventors: Dimiter S. Dimitrov (NCI) *et al.*

Publication: Feng Y, Xiao X, Zhu Z, Dimitrov D. Identification and characterization of a novel agonistic anti-DR4 human monoclonal antibody. MAbs. 2010 Sep-Oct;2(5):565–570. [PubMed: 20581445]

Patent Status: U.S. Provisional Application No. 61/355,449 filed 16 Jun 2010 (HHS Reference No. E–158–2010/0–US–01)

Licensing Status: Available for licensing.

Licensing Contact: Whitney Hastings; 301–451–7337; *hastingw@mail.nih.gov.*

Collaborative Research Opportunity: The National Cancer Institute, Membrane Structure and Function Section, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize topic of invention or related laboratory interests. Please contact John Hewes, PhD at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Gene Signature for Predicting Solid Tumors Patient Prognosis

Description of Technology: A progressive sequence of somatic mutations and epigenetic changes of oncogenes or tumor suppressor genes are believed to cause tumor development. However, high genomic instability in tumors causes the accumulation of genomic aberrations that do not contribute to tumor progression. Therefore it is important to distinguish between 'driver' mutations which are functionally important and 'passenger' mutations which do not provide a selective advantage to the tumor cells.

The current invention describes a driver gene signature for predicting survival in patients with solid malignancies including hepatocellular carcinoma (HCC) and breast cancer. The gene signature includes ten cancer-associated genes, and the NIH researchers further discovered that a decrease in DNA copy number or mRNA expression of some genes is associated with poor prognosis in HCC tumors and breast cancer, while a decrease in DNA copy number or mRNA expression of a few other genes is associated with good prognosis. They have also demonstrated that at least four of these cancer-associated genes are functional tumor suppressor genes. Thus, these genes may be potential molecular targets of HCC and breast cancer.

Available for licensing is a method of predicting the prognosis of a patient diagnosed with HCC or breast cancer by detecting expression of one or more cancer-associated genes, and a method of identifying an agent for use in treating HCC.

Applications:

• Prognosis for hepatocellular carcinoma (HCC) and breast cancer patient survival.

• Potential new method to identify therapeutic treatment for HCC and breast cancer patients.

Development Status: Early-stage development.

Market:

• Hepatocellular carcinoma (HCC) is the most frequent malignant tumor in the liver and the third leading cause of cancer death worldwide. Systemic chemotherapy has been shown to be ineffective and tumor recurrence rate after surgical resection is high due to relapse and metastasis. Therefore, the development of new drugs will be crucial to prevent relapse and to prolong patient survival.

• Breast cancer

Inventors: Dr. Xin Wei Wang and Dr. Stephanie Roessler (NCI)

Patent Status:

• U.S. Provisional Application No. 61/198,813 filed 10 Nov 2008 (HHS Reference No. E–024–2009/0–US–01)

• PCT Application No. PCT/US2009/063883 filed 10 Nov 2009, which published as WO 2010/054379 on 14 May 2010 (HHS Reference No. E–024–2009/0–PCT–02)

Licensing Status: Available for licensing.

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

Collaborative Research Opportunity: The National Cancer Institute, 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 this Gene Signature for Predicting Hepatocellular Carcinoma Patient Prognosis. Please contact John Hewes, PhD at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Prevention of Head and Neck Cancer Using Rapamycin and Its Analogs

Description of Technology: It is frequently observed in head and neck squamous cell carcinoma (HNSCC), a cancer occurring mostly in the mouth, that the Akt/mTOR pathway is abnormally activated. Therefore, inhibiting this signaling pathway may help in treating this disease. Rapamycin and its analogs are known to inhibit the activity of mTOR so in principle they could serve as therapeutics for treating HNSCC.

Researchers at the NIH have developed a method of potentially preventing or treating HNSCC through the inhibition of mTOR activity. The proof of this principle was demonstrated by rapid regression of mouth tumors in mice afflicted with Cowden syndrome with the administration of rapamycin. Like HNSCC, development of this disease is linked to over activation of the Akt/mTOR pathway. Furthermore, the therapeutic potential of rapamycin was demonstrated using mice in experiments that model chronic exposure to tobacco, which promotes the development of HNSCC. Therefore, inhibitors of mTOR have considerable potential in the prevention and treatment of HNSCC.

Applications: Preventing the development of oral cancer using mTOR inhibitors to halt progression of pre-cancerous lesions.

Development Status: Pre-clinical proof of principle.

Market:

• Approximately 500,000 new cases of squamous cell carcinomas of the head and neck arise every year making it the 6th most common cancer in the world.

• Frequently, prognosis is poor due to late detection of cancer.

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

Publications:

1. Squarize CH, Castilho RM, Gutkind JS. Chemoprevention and treatment of experimental Cowden's disease by mTOR inhibition with rapamycin. Cancer Res. 2008 Sep 1;68(17):7066–7072. [PubMed: 18757421]

2. Czerninski R, Amornphimoltham P, Patel V, Molinolo AA, Gutkind JS. Targeting mTOR by rapamycin prevents

tumor progression in an oral-specific chemical carcinogenesis model. Cancer Prevention Res. 2009 Jan;2(1):27–36. [PubMed: 19139015]

3. Raimondi AR, Molinolo A, Gutkind JS. Rapamycin prevents early onset of tumorigenesis in an oral-specific K-ras and p53 two-hit carcinogenesis model. Cancer Res. 2009 May 15;69(10):4159–4166. [PubMed: 19435901]

Patent Status: U.S. Patent Application No. 13/059,335 filed August 20, 2009 (HHS Reference No. E–302–2008/0–US–05) and related international filings

Related Technology: International Application No. PCT/IL2010/000694 filed August 25, 2010 (HHS Reference No. E–282–2009/0–PCT–02), entitled "Prevention and Treatment of Oral and Lips Diseases Using Sirolimus and Derivatives Sustained Release Delivery Systems for Local Application to the Oral Cavity and Lips"

Licensing Status: Available for licensing.

Licensing Contact: Whitney Hastings; 301–451–7337; *hastingw@mail.nih.gov*

Collaborative Research Opportunity: The National Institute of Dental and Craniofacial Research, Oral and Pharyngeal Cancer Branch, 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 *bradleyda@nidcr.nih.gov* for more information.

Three-Dimensional Co-Culture Assay System for Angiogenesis and Metastasis

Description of Technology: This technology features an assay for the detection and measurement of angiogenesis (formation of new blood vessels) and metastasis (spread of cancer). The inventors have developed a three-dimensional co-culture system that closely mimics the *in vivo* environment in which angiogenesis and metastatic tumors develop. The co-culture system consists of cancerous cells (tumor spheroid or biopsy), endothelial cells, and a combination of other mammalian cells (mast cells, adipocytes, fibroblasts, macrophages, *etc.*). The cancerous cells can be obtained from cell lines or biopsied tumors from various cancers, such as melanoma, ovarian cancer, hepatocellular cancer, or colon cancer. Cells in the three-dimensional co-culture system express a fluorescent protein having a different emission spectrum. Consequently, the co-culture systems can be used to identify, monitor, and measure changes in morphology, migration, proliferation and apoptosis of cells involved in angiogenesis and/or metastasis. The co-cultures are developed in 96-well plates to allow rapid and efficient screening for whether a drug impacts multiple cell types, modulates angiogenesis and/or has a therapeutic impact on metastasis. This technology not only represents an important tool for angiogenesis and cancer research, but also may be developed into a diagnostic test that allows the development of personalized therapies for cancer and other angiogenesis-mediated disease.

Applications:

- Personalized therapies for cancer and other angiogenesis-mediated diseases
- Screening for cytotoxic compounds, modulators of angiogenesis, and anti-metastatic compounds
- Basic research applications, such as fluorescence-activated cell sorting (FACS), time-lapse cinematography, and confocal microscopy

Advantages:

- Closely mimics tumor microenvironment
- Efficient screening method for basic research, drug discovery and for clinical use

Development Status: Experimental data available; inventors have also developed a high-throughput screening assay based on this technology

Inventors: Changge Fang, Enrique Zudaire, Frank Cuttitta (NCI)

Patent Status:

- U.S. Provisional Application No. 60/976,732 filed 01 Oct 2007 (HHS Reference No. E–281–2007/0–US–01)
- U.S. Application No. 12/802,666 filed 10 Jun 2010 (HHS Reference No. E–281–2007/1–US–01)

Licensing Status: Available for licensing.

Licensing Contact: Tara L. Kirby, PhD; 301.435.4426; *kirbyt@mail.nih.gov.*

Collaborative Research Opportunity: We are very interested in setting up collaborations with pharmaceutical, biomedical, or academic investigators to use our technology in the form of a CRADA or joint grant submission (*e.g.* DOD). These studies could include expanding the complexity of a 3D co-culture by increasing the partner cell number—paralleling the current model of in vivo angiogenesis. Our existing co-culture assay incorporates both immortalized tumor and endothelial cells. However, other anatomically distinct cells could be added (*e.g.* pericytes, inflammatory cells [mast cell or macrophages], or fibroblasts) to more accurately mimic the in vivo setting. In addition, a more thorough analysis of our prior xenograft biopsy studies for assessing drug sensitivity could be done using a variety of human tumor cell lines that include lung, colon, breast, prostate, and ovarian cancer. Finally, this collaboration would segue into clinical studies taking biopsy material from cancer patients (following approved IRB protocols) to evaluate anti-angiogenic drug sensitivities to determine the most appropriate FDA reviewed/certified anti-cancer drugs.

The National Cancer Institute, Radiation Oncology Branch, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology as noted above. Please contact John Hewes, PhD at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Dated: March 15, 2011.

Richard U. Rodriguez,

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

[FR Doc. 2011–6570 Filed 3–18–11; 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.

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Synthetic Peptide Inhibitors of the Wnt Pathway

Description of Technology: Available for licensing are peptide inhibitors of