## 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.

**Method for Detection and Quantification of PLK1 Expression and Activity**

*Description of Technology:* Polo-like kinase 1 (Plk1) plays a role in the regulation of the cell cycle and control of cellular proliferation. Because Plk1 is associated with neoplastic transformation of human cells, expression of this protein has been proposed as a prognostic marker for many types of malignancies. In mammalian cells, four Plks exist, but their expression patterns and functions appear to be distinct from each other. Available for licensing is a Plk1 ELISA assay using peptide substrates that are specific for Plk1, in that they are phosphorylated and bound by Plk1, but not by the related polo kinases Plk2, Plk3 and Plk4.

By exploiting a unique Plk1-dependent phosphorylation and binding property, an easy and reliable ELISA assay has been developed to quantify Plk1 expression levels and kinase activity. With this highly sensitive assay, Plk1 activity can be measured with 2–20 microgram of total lysates without immunoprecipitation or purification steps. Since deregulated Plk1 expression has been suggested as a prognostic marker for a wide range of human malignancies, this assay may provide an innovative tool for assessing the predisposition for cancer development, monitoring cancer progression, and estimating the prognosis of various types of cancer patients.

*Applications:* Optimized PBIP1 polypeptides, a natural substrate of Plk1, with enhanced specificity and sensitivity over the native PBIP1 sequence.

ELISA assay to quantify Plk1 expression and kinase activity.

*Advantages:* Rapid, highly sensitive assay that requires lower amounts of starting material than conventional immunoprecipitation assays.

Assay that is selective for Plk1.

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

*Market:* An estimated 1,444,920 new cancer diagnoses in the U.S. in 2007. Cancer is the second leading cause of death in United States. It is estimated that the cancer therapeutic market would double to $50 billion a year in 2010 from $25 billion in 2006.

*Inventors:* Kyung Lee and Jung-Eun Park (NCI).

*Publications:* 1. J-E Park, L Li, K Strebhardt, SH Yuspa, and KS. Lee. Direct quantification of polo-like kinase 1 activity in cells and tissues using a highly sensitive and specific ELISA assay (about to be submitted).

2. KS Lee et al. Mechanisms of mammalian polo-like kinase 1 (Plk1) localization: self-versus non-self-priming. Cell Cycle 2008 Jan;7(2): 141–145.

3. KS Lee et al. Self-regulated mechanism of Plk1 localization to kinetochores: lessons from the Plk1–PBIP1 interaction. Cell Div. 2008 Jan 23;3:4.

4. YH Kang et al. Self-regulated Plk1 recruitment to kinetochores by the Plk1–PBIP1 interaction is critical for proper chromosome segregation. Mol Cell. 2006 Nov 3;24(3): 409–422.

*Patent Status:* U.S. Provisional Application No. 61/054,032 filed 16 May 2008 (HHS Reference No. E–091–008/0–US–01).

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

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

*Collaborative Research Opportunity:* The National Cancer Institute, Laboratory of Metabolism is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize the PLK1 ELISA assay described above. Please contact John D. Hewes, Ph.D. at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

**Cripto-1 Represents a Biomarker for Chronic Inflammatory Diseases**

*Description of Technology:* Chronic inflammatory bowel disease (IBD) (*e.g.* Crohn's disease and ulcerative colitis) and chronic inflammatory arthropathy such as rheumatoid arthritis represent an enormous socio-economic burden due to the cost for long term medication and rehabilitation and the decreased productivity due to periods of acute recurrences. A major characteristic of these diseases is the tissue infiltration of specific CD4+ T cells that sustain inflammation by secreting cytokines. One of these cytokines, TNF-alpha, is a current therapeutic target for the treatment of these chronic inflammatory diseases.

This technology describes Cripto-1 as a biomarker for chronic inflammatory diseases. Cripto-1, an epidermal growth factor (EGF)-related protein, shows higher expression levels in tissue sections of Crohn's disease, ulcerative colitis, and rheumatoid arthritis as compared to adjacent unaffected areas. Moreover, the inventors show that the response to Cripto-1 is not due to a generic immune response, and Cripto-1 expression increases the expression of TNF-alpha in CD4+ T cells in tissues affected by chronic inflammatory disease. As a result, this technology could be used as a diagnostic biomarker for chronic inflammatory diseases as well as a novel therapeutic target to help control TNF-alpha in chronic inflammatory diseases.

*Applications:* Diagnostic tool for the detection of a chronic inflammatory disease.

Method to inhibit cytokine production in a tissue affected with a chronic inflammatory disease.

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

*Inventors:* Luigi Strizzi, David S. Salomon, Monica I. Gonzales (NCI).

*Patent Status:* U.S. Provisional Application No. 61/045,746 filed 17 Apr 2008 (HHS Reference No. E–075–2008/0–US–01).

*Licensing Status:* Available for licensing.

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

*Collaborative Research Opportunity:* The National Cancer Institute Mammary Biology and Tumorigenesis Laboratory is seeking statements of capability or interest from parties interested in collaborative research to further

develop, evaluate, or commercialize Cripto-1 as a biomarker for chronic inflammatory diseases. Please contact John D. Hewes, Ph.D. at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

**Cripto-1 as a Biomarker for Cardiac Ischemia**

*Description of Technology:* Ischemic heart disease is a major cause of human cardiac morbidity and mortality, affecting over 14 million people in the United States alone. Current detection of cardiac ischemia relies upon identification of electrocardiographic anomalies and the release of cardiac markers from the damaged myocardial tissue. Unfortunately, patients with acute myocardial infarction are often insensitive to these tests during the early phases of intervention and as a result more markers for cardiac ischemic disease are needed.

This technology describes Cripto-1 as a biomarker for infarcted cardiac tissues. Cripto-1 is a member of the epidermal growth factor (EGF)-related proteins and is currently thought to play an important role in several cancers. The present invention shows that Cripto-1 is overexpressed in infarcted myocardial tissue, and not expressed or weakly expressed in non-infarct related heart disease tissues and normal tissues. Furthermore, the overexpression of Cripto-1 correlates with the hypoxia-inducible factor-1-alpha indicating specificity to ischemic heart tissue. The expression of Cripto-1 has also been shown to be highly expressed in stem cells, which may have an important role in the repair of damaged myocardial tissue. Thus, this technology could represent a new biomarker for the diagnosis of myocardial infarction as well as a surrogate biomarker to monitor the healing process including regenerative stem cell activity of the infarcted myocardial tissue.

*Applications:*

Diagnostic tool for the detection of myocardial infarction.

Method to monitor stem cell activity in damaged myocardial tissue.

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

*Inventors:* Luigi Strizzi, Caterina Bianco, David S. Salomon (NCI).

*Patent Status:* U.S. Provisional Application No. 61/046,181 filed 18 Apr 2008 (HHS Reference No. E–049–2008/0-US–01).

*Licensing Status:* Available for licensing.

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

*Collaborative Research Opportunity:* The National Cancer Institute Mammary Biology and Tumorigenesis Laboratory is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize Cripto-1 as a biomarker for cardiac ischemia. Please contact John D. Hewes, Ph.D. at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

**Identification of Persons Likely To Benefit From Statin Mediated Cancer Prevention by Pharmacogenetics**

*Description of Technology:* Inhibitors of 3-hydroxy-3-methylglutaryl (HMG) coenzyme A reductase (statins) are a class of well-tolerated compounds that are the most widely used cholesterol-lowering drugs in the United States. Reduced cancer risk among statin users has also been observed as a secondary outcome in randomized controlled clinical trials evaluating effects of statins on cardiovascular outcomes. However the observed cancer risk reduction varied with different clinical studies. Thus there is a need to identify individuals who would benefit from treatment with statins.

The current invention describes a pharmacogenetic method to identify candidates who are most likely to benefit from treatment with statins to reduce cancer risk, and consequently minimizing any unnecessary cost and side effects in individuals who do not benefit. Specifically, we discovered that an HMGCR genetic variant rs12654264 is associated with significantly lower colorectal cancer risk, with most of the benefit seen in HMGCoA reductase inhibitor (statin) users. We also discovered that this same HMGCR genetic variant is associated with significantly higher serum cholesterol levels in Israeli colorectal cancer patients. The same HMGCR genetic variant has also been associated with significantly higher serum cholesterol levels in two independent groups of individuals of mixed European descent [*http://www.broad.mit.edu/diabetes/scandinavs/index.html* and *N Engl J Med.* 2008 March 20;358(12):1240–1249 (*http://www.ncbi.nlm.nih.gov/pubmed/18354102?dopt*)]. These data suggest that the same genetic variant modifies cholesterol metabolism in a manner that affects both colorectal cancer risk and cardiovascular risk.

*Applications and Market:* Statins account for approximately 80% of the cholesterol-lowering drugs prescribed in the United States, and six statins are currently available on the U.S. market. Reduced cancer risk is also associated with statin use. This invention provides a method to indentify individuals who are most likely to benefit from cancer chemopreventive treatment with statins.

Pharmacogenetic markers can be developed to identify patient population that can benefit from statins, therefore expanding the markets of stains.

*Development Status:* The inventors have discovered several novel genetic variants of HMG coenzyme A reductase gene, and are further investigating the functional significance of the variants in vitro.

*Inventors:* Dr. Levy Kopelovich (NCI) et al.

*Patent Status:* U.S. Provisional Application No. 60/985,587 filed 05 Nov 2007 (HHS Reference No. E–328–2007/0–US–01).

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

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

**TGF-beta Gene Expression Signature in Cancer Prognosis**

*Description of Technology:* Hepatocellular carcinoma (HCC) is the third leading cause of cancer death worldwide, and it is very heterogeneous in terms of its clinical presentation as well as genomic and transcriptomic patterns. This heterogeneity and the lack of appropriate biomarkers have hampered patient prognosis and treatment stratification.

Available for licensing is a novel temporal TGF-beta gene expression signature that predicts HCC patient clinical outcomes. Patients with tumors expressing late TGF-beta responsive genes had a malignant prognosis and an invasive tumor phenotype as evaluated by decreased survival time, increased tumor recurrence, and vascular invasion rate. Additionally, this signature may also be able to prognose other cancers, including lung cancer.

*Applications:* Method to diagnose cancer.

Method to monitor cancer progression and aid clinicians to choose appropriate therapies.

Commercial kits to prognose cancer.

*Advantages:* Early diagnostic tool to stratify HCC patients to chose more effective treatment.

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

*Market:* An estimated 1,444,920 new cancer diagnosed in the U.S. in 2007.

Cancer is the second leading cause of death in United States.

It is estimated that the cancer therapeutic market would double to $50 billion a year in 2010 from $25 billion in 2006.

*Inventors:* Snorri Thorgeirsson (NCI) and Cedric Coulouaran (NCI)

*Relevant Publication:* Coulouaran C, Factor VM, Thorgeirsson SS. Transforming growth factor-beta gene expression signature in mouse hepatocytes predicts clinical outcome in human cancer. Hepatology 2008 Jun;47(6):2059–2067.

*Patent Status:* U.S. Provisional Application No. 60/981,661 filed 22 Oct 2007 (HHS Reference No. E–282–2007/0-US–01)

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

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

*Collaborative Research Opportunity:* The National Cancer Institute, Center for Cancer Research, Laboratory of Experimental Carcinogenesis is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize a novel temporal TGF-beta gene expression signature that predicts HCC patient clinical outcomes. Please contact John D. Hewes, PhD at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

**A New Pot1 Variant Gene as a Diagnostic Biomarker for Hereditary Non-polyposis Colorectal Cancer**

*Description of Technology:* The diagnosis of Hereditary Nonpolyposis Colorectal Cancer (HNPCC) is difficult because the disease lacks phenotypic signs that might facilitate its presymptomatic diagnosis. This invention is based on the identification of a new splice variant of a gene that appears to exist specifically in HNPCC, namely ''Pot1'' or ''Protection of Telomeres.'' Pot1 has a critical role in ensuring chromosome stability by binding to telomeres. The invention presents a variant of Pot1 that is present in mismatch repair-deficient, but not proficient, cancer cell lines and primary, non-tumor tissue samples. The presence of this variant may be useful both as a diagnostic marker for HNPCC, and as a new therapeutic target for the treatment of HNPCC.

*Applications and Modality:* Identification of new ''Pot1'' variant gene associated with HNPCC

New gene can be used as a potential diagnostic biomarker for the diagnosis of HNPCC.

Pot1 as a new therapeutic target for the treatment of HNPCC.

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

*Inventors:* Qin Yang and Curtis C. Harris (NCI).

*Related Publications:*

1. P Baumann *et al.* Human Pot1 (protection of telomeres) protein: cytolocalization, gene structure, and alternative splicing. Mol Cell Biol. 2002 Nov;22(22):8079–8087.

2. A Umar *et al.* Revised Bethesda Guidelines for hereditary nonpolyposis colorectal cancer (Lynch syndrome) and microsatellite instability. J Natl Cancer Inst. 2004 Feb 18;96(4):261–268.

3. HT Lynch *et al.* Hereditary nonpolyposis colorectal carcinoma (HNPCC) and HNPCC-like families: Problems in diagnosis, surveillance, and management. Cancer. 2004 Jan 1;100(1):53–64.

4. Q Yang *et al.* Functional diversity of human protection of telomeres 1 isoforms in telomere protection and cellular senescence. Cancer Res. 2007 Dec 15;67(24):11677–11686.

*Patent Status:* U.S. Provisional Application No. 60/620,754 filed 20 Oct 2004 (HHS Reference No. E–263–2004/0–US–01), entitled ''POT1 Alternating Splice Variants''

International Patent Application No. PCT/US2005/037957 filed 19 Oct 2005, which published as WO 2006/045062 on 27 Apr 2006 (HHS Reference No. E–263–2004/0–PCT–02)

U.S. Patent Application No. 11/665,944 filed 20 Apr 2007 (HHS Reference No. E–263–2004/0-US–03).

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

*Licensing Contact:* Surekha Vathyam, PhD; 301–435–4076; *vathyams@mail.nih.gov*.

*Collaborative Research Opportunity:* The National Cancer Institute Laboratory of Human Carcinogenesis is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize biomarkers of colon cancer. Please contact John D. Hewes, PhD at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Dated: June 30, 2008.

**Richard U. Rodriguez,**

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

[FR Doc. E8–15562 Filed 7–8–08; 8:45 am]

**BILLING CODE 4140–01–P**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### National Institutes of Health

### Center for Scientific Review; Notice of Closed Meetings

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meetings.

The meetings will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(cX6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

*Name of Committee:* Center for Scientific Review Special Emphasis Panel, Gene Therapy and Inborn Errors-2.

*Date:* July 14, 2008.

*Time:* 1 p.m. to 5 p.m.

*Agenda:* To review and evaluate grant applications.

*Place:* National Institutes of Health, 6701 Rockledge Drive, Bethesda, MD 20892. (Telephone Conference Call)

*Contact Person:* Richard Panniers, PhD, Scientific Review Officer, Center for Scientific Review, National Institutes of Health, 6701 Rockledge Drive, Room 2212, MSC 7890, Bethesda, MD 20892, (301) 435–1741, *pannierr@csr.nih.gov.*

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

*Name of Committee:* Center for Scientific Review Special Emphasis Panel, Review of Member Conflict Applications from BSPH and ACE.

*Date:* July 28, 2008.

*Time:* 10 a.m. to 2 p.m.

*Agenda:* To review and evaluate grant applications.

*Place:* National Institutes of Health, 6701 Rockledge Drive, Bethesda, MD 20892. (Telephone Conference Call)

*Contact Person:* Mark P. Rubert, PhD, Scientific Review Officer, Center for Scientific Review, National Institutes of Health, 6701 Rockledge Drive, Room 5218, MSC 7852, Bethesda, MD 20892, 301–435–1775, *rubertm@csr.nih.gov.*

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

(Catalogue of Federal Domestic Assistance Program Nos. 93.306, Comparative Medicine; 93.333, Clinical Research, 93.306, 93.333, 93.337, 93.393–93.396, 93.837–93.844, 93.846–93.878, 93.892, 93.893, National Institutes of Health, HHS)

Dated: July 1, 2008.

**Jennifer Spaeth,**

*Director, Office of Federal Advisory Committee Policy.*

[FR Doc. E8–15469 Filed 7–8–08; 8:45 am]

**BILLING CODE 4140–01–M**