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.

T-Cell Enumeration Using Dried Blood Spots as a Surrogate for CD4+ T-Cell Counts To Monitor HIV+ Patients

Description of Technology: Available for licensing and commercial development is a novel method for enumerating T-cells in HIV+ patients using dried blood spots, avoiding the need for fresh blood samples. The method relies on the distinctive nature of the TCR–β gene, which undergoes a rearrangement during T-cell development that is required to produce a functional T-cell receptor protein. Since only mature T-cells contain a rearranged TCR–β gene, the method quantifies the number of T-cells in a patient sample by quantifying the number of cells that contain a rearranged TCR–β gene. In addition to dried blood spots, the assay can be also used with a wide variety of sample types from which T-cell counts were previously impossible to obtain, such as swabs and tissue slides. In addition, this method can be used for monitoring of a variety of T-cell leukemias/lymphomas, and easily adapted to monitor B-cell levels found in B-cell leukemias/lymphomas.

The assay was found to accurately predict TCR–β levels ($r=0.985$, $p<0.0001$), and to correlate well with known CD4 counts ($r=0.670$, $p<0.0001$). Therefore, this novel method can be used to monitor HIV infection in order to determine antiretroviral therapy (ART) initiation and monitoring. A large international effort has been made to provide ART to the more then 33 million HIV+ people worldwide, but significant hurdles remain to large-scale implementation due to the lack of medical and laboratory infrastructure found in the developing world, where the majority of HIV+ individuals are found. In particular, a CD4 count, which requires fresh whole blood, a reliable cold-transport chain, and an expensive FACS based reader, is required to monitor patients and determine ART initiation. This requirement has become one of the largest impediments to expanding ART around the world. Therefore, this novel method provides a superior functional assay for HIV disease staging that does not require cold storage or fresh sample processing. Dried blood spots are an ideal sample collection method for large scale monitoring in the developing world due to the relatively simple manner in which samples can be obtained and the high stability of the sample in the absence of refrigeration. This method provides an easier and less expensive method for HIV monitoring for the developing world, and could be also used as an at home monitoring system for HIV-infected patients in developed countries.

Development Status: Fully developed and testing in HIV+ subjects has been performed with successful results.

Inventors: Andrew D. Redd and Thomas C. Quinn (NIAID).

Relevant Publication: A manuscript describing the above technology will be available as soon as it is accepted for publication.

Patent Status: U.S. Provisional Patent Application No. 61/131,954, filed 12 June 2008, entitled ''Monitoring TCR–β to Determine HIV Therapy and Disease Progression'' (HHS Reference No. E–203–2008/0–US–01).

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

Licensing Contact: Cristina Thalhammer-Reyero, PhD, MBA; 301–435–4507; *thalhamc@mail.nih.gov*.

Collaborative Research Opportunity: The National Institute of Allergy and Infectious Diseases, Laboratory of Immunoregulation, International HIV and STD Unit, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize TCR–β enumeration to monitor HIV+ patients, as well as other diseases or syndromes in which T-cell monitoring is commonly performed. Please contact Andrew Redd, PhD, at 410–614–0813 or *aredd2@jhmi.edu* for more information.

Metabolic Biomarkers Indicate Exposure to Gamma Radiation

Description of Technology: Available for licensing and commercial development are methods of diagnosing exposure to gamma radiation in a mammal. Gamma radiation has both short-term and long-term adverse health effects including cancer. Urine samples collected from exposed mouse models irradiated at 0, 3, and 8 Gy (2.57 Gy/min) were analyzed by ultra-performance liquid chromatography-time of flight mass spectrometry (UPLC–TOFMS). Statistical analysis revealed that the following metabolomic markers were associated with exposure: 2′-deoxyxanthosine, xanthosine, 2′-deoxyuridine, 2′-deoxycytidine, N-hexanoylglycine and P-thymidine are urinary biomarkers of 3 and 8 Gy exposure. 3-hydroxy-2-methylbenzoic acid 3-O-sulfate and xanthine are elevated in urine of mice exposed to 3 but not 8 Gy, and taurine is elevated after 8 but not 3 Gy exposure.

Applications: Radiation Exposure; Metabolomics.

Inventors: Frank J. Gonzalez (NCI), John Tyburski (NCI), Kristopher Krausz (NCI), Andrew Patterson (NIGMS), *et al.*

Publications:

1. Patterson AD, Li H, Eichler GS, Krausz KW, Weinstein JN, Fornace AJ, Gonzalez FJ, Idle JR. UPLC–ESI–TOFMS-based metabolomics and gene expression dynamics inspector self-organizing metabolomic maps as tools for understanding the cellular response to ionizing radiation. Anal Chem. 2008 Feb 1;80(3):665–674.

2. Tyburski JB, Patterson AJ, Krausz KW, Slavk J, Fornace AJ, Gonzalez FJ, Idle JR. Radiation metabolomics: Identification of minimally invasive urine biomarkers for gamma radiation exposure in mice. Radiat Res. 2008 Jul;170(1):1–14.

Patent Status: U.S. Patent Application No. 12/121,208 filed 15 May 2008 (HHS Reference No. E–070–2008/0–US–01).

Licensing Status: Available for licensing.

Licensing Contact: Michael A. Shmilovich, Esq.; 301–435–5019; *shmilovm@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 development of

biomarkers for radiation gamma exposure and cell damage. Please contact John D. Hewes, PhD, at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Dated: July 17, 2008.

Richard U. Rodriguez,

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

[FR Doc. E8–17021 Filed 7–24–08; 8:45 am]

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Prolactin Receptor Antibodies as a Diagnostic Marker and Therapeutic Agent for Cancer

Description of Technology: Prolactin is a key hormone in the normal breast development and plays a role in the growth and development of other major organs such as the prostate. The biologic function of prolactin is mediated by specific receptors on the cell surface, with breast cancer cells containing more receptors than normal tissue. The prolactin receptor, a member of the large class-1 cytokine receptor superfamily, has three major isoforms that are cell associated. The specific isoform concentration and distribution determines biological activity and may determine susceptibility to antiprolactin drugs.

This technology describes several antibodies, both polyclonal and monoclonal, to the prolactin receptor. These include antibodies to the three major isoforms: the long isoform (LF), two short isoforms (SF1a and SF1b), and the secreted form, prolactin receptor Δ7–11. These antibodies can be used for the diagnosis of prolactin sensitive tumors. Furthermore, the presence of the secreted prolactin receptor Δ7–11 may provide a blood test for prolactin responsive tumors.

Applications:

• Diagnostic tool for the detection of prolactin sensitive tumors.

• Antibodies as a serum diagnostic in high-throughput assays.

• Conjugated antibodies used in targeted therapy of cancer.

Market:

• In the U.S. over 2 million women have been treated for breast cancer and with more than 200,000 women diagnosed in the year 2007 alone. Breast cancer is the second leading cause of cancer death in women.

• Prostate cancer is the most common type of cancer found in American men, and it has been estimated that there were more than 230,000 new cases in the U.S. in 2007. Prostate cancer is also the second leading cause of cancer death in men.

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

Inventors: Barbara Vonderhaar, Erika Ginsburg, Paul Goldsmith (NCI).

Patent Status: HHS Reference No. E–232–2008/0—Research Material. Patent protection is not being pursued for this technology.

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 isoform specific antibodies to the human prolactin receptor. Please contact John D. Hewes, PhD, at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Mouse Embryonic Stem Cell-Based Functional Assay To Evaluate Mutations in BRCA2

Description of Technology: Mutations in breast cancer susceptibility genes BRCA1 and BRCA2 have up to an 80% life time risk in developing breast cancer. There are no ''mutation hot spots'' and to date, more than 1,500 different mutations have been identified in BRCA2. The absence of tumor cell lines expressing various mutant BRCA2 alleles has hindered evaluations to determine the functional differences between different mutations.

A simple, versatile and reliable mouse embryonic stem cell and bacterial artificial chromosome based assay to generate cell lines expressing mutant human BRCA2 has been developed and it has been used to classify 17 sequence variants. Available for licensing are a wild-type and eleven mutant BRCA2 cell lines developed from this assay that have either truncations or point mutations. These cell lines may be used to evaluate the effect of DNA damaging agents, genotoxins and chemotherapeutic efficacy.

Applications:

• Research tool to generate and study BRCA2 mutations.

• Method to screen for chemotherapeutics.

• Method to evaluate DNA damaging agents.

Advantages: Ready to use portfolio of BRCA2 mutant cell lines to study BRCA2 mutant functional analysis.

Market: An estimated 180,510 new cases of breast cancer will be diagnosed and may cause 40,480 deaths in the U.S. in 2008.

Inventors: Shyam K. Sharan and Sergey Kuznetsov (NCI).

Publication: SG Kuznetsov *et al.* Mouse embryonic stem cell-based functional assay to evaluate mutations in BRCA2. Nat Med. 2008, in press. Published online 11 July 2008, doi:10.1038/nm.1719.

Patent Status: HHS Reference No. E–261–2007/0—Research Tool. Patent protection is not being pursued for this technology.

Licensing Status: Available for biological materials licensing only.

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

Collaborative Research Opportunity: The Mouse Cancer Genetics Program, Center for Cancer Research, National Cancer Institute, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize mouse embryonic stem cell lines suitable for functional analysis of BRCA2 variants. Please contact John D. Hewes, PhD, at 301–435–3121 or *hewesj@mail.nih.gov* for more information.