DEPARTMENT OF HEALTH AND HUMAN SERVICES

Centers for Disease Control and Prevention

Draft Guideline for Prevention of Catheter-Associated Urinary Tract Infections 2008

AGENCY: Centers for Disease Control and Prevention (CDC), Department of Health and Human Services (DHHS).

ACTION: Notice of document availability and request for public comment.

SUMMARY: This notice is a request for review of and comment on the *Draft Guideline for Prevention of Catheter-Associated Urinary Tract Infections 2008,* available on the following Web site: *http://wwwnd.cdc.gov/publiccomments/.* This document is for use by infection prevention staff, healthcare epidemiologists, healthcare administrators, nurses, other healthcare providers, and persons responsible for developing, implementing, and evaluating infection prevention and control programs for healthcare settings across the continuum of care. The guideline updates and expands the 1981 Guideline for Prevention of Catheter-associated Urinary Tract Infections.

DATES: Comments must be received on or before July 6, 2009.

ADDRESSES: Comments on the *Draft Guideline for Prevention of Catheter-Associated Urinary Tract Infections* should be submitted by e-mail to *cauti@cdc.gov* or by mail to CDC, Division of Healthcare Quality Promotion, Attn: Resource Center, 1600 Clifton Rd., NE., Mailstop A–31, Atlanta, Georgia 30333; or by fax 404–639–4049.

SUPPLEMENTARY INFORMATION: The *Draft Guideline for Prevention of Catheter-Associated Urinary Tract Infections* addresses prevention of CAUTI for patients in need of either short- or long-term urinary catheterization in any type of healthcare setting and includes data for indwelling urethral catheterization as well as alternative methods of urinary drainage. The guideline also includes specific recommendations for implementation, performance measurement, and surveillance. Recommendations for further research are also included to address the knowledge gaps in CAUTI prevention identified during the literature review. The guideline is based on a targeted systematic review of the best available evidence with explicit links between the evidence and recommendations.

Dated: May 21, 2009.

James D. Seligman,

Chief Information Officer, Centers for Disease Control and Prevention.

[FR Doc. E9–12901 Filed 6–2–09; 8:45 am]

BILLING CODE 4163–18–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.

Novel Method of Treating Cancer Using Ixolaris

Description of Technology: Aggressive tumors spread between tissues in a process known as metastasis. Tumor metastasis, particularly with regard to brain cancer (gliomas), has been linked to the aberrant expression of membrane-bound tissue factor (TF). TF normally functions as a blood coagulation factor and can lead to the production of pro-angiogenesis factors such as vascular endothelial growth factor (VEGF). By doing this in the vicinity of tumors, TF may enhance both tumor growth and the ability of tumors to metastasize.

Ixolaris is a protein that prevents the initiation of blood coagulation, specifically by inhibiting TF. NIH inventors have explored the possibility that Ixolaris could be effective as an anti-cancer therapy. As an inhibitor of TF, Ixolaris could potentially inhibit the function of TF, thereby reducing the ability of a tumor to develop and to metastasize. Recent data show that Ixolaris has the ability to prevent tumor growth in vivo using mouse xenograft models. Importantly, the inhibition in vivo occurred without noticeable bleeding. Since Ixolaris is not immunogenic, it might be an excellent candidate as an anti-cancer therapeutic.

Application: Treatment and prevention of tumor growth and metastasis by inhibiting TF and blood vessel formation.

Advantages: Provides a novel mechanism for preventing tumor metastasis.

Development Status: Preclinical stage of development.

Inventors: Ivo Francischetti (NIAID) *et al.*

Patent Status: U.S. Provisional Application No. 61/161,223 (HHS Reference No. E–148–2009/0–US–01).

For more information, see:

1. U.S. Patent 7,078,508 entitled ''Ixodes Scapularis Tissue Factor Pathway Inhibitor''.

2. IM Francischetti et al. Ixolaris, a novel recombinant tissue factor pathway inhibitor (TFPI) from the salivary gland of the tick, Ixodes scapularis: identification of factor X and factor Xa as scaffolds for the inhibition of factor VIIa/tissue factor complex. Blood 2002 May 15;99(10):3602–3612.

3. RA Nazareth *et al.* Antithrombotic properties of Ixolaris, a potent inhibitor of the extrinsic pathway of the coagulation cascade. Thromb Haemost. 2006 Jul;96(1):7–13.

Licensing Status: Available for licensing.

Licensing Contact: David A. Lambertson, PhD; 301–435–4632; *lambertsond@mail.nih.gov.*

Collaborative Research Opportunity: The NIAID, OTD, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize Ixolaris for cancer treatment. Please contact Dana Hsu at 301–496–2644 for more information.

Immortalized Virus-Free Human Placental Cell Lines

Description of Technology: This technology provides immortalized virus-free human placental cell lines. To develop these cell lines, human placental cells were immortalized with adenovirus-origin-minus (ori-)-simian virus-40 (SV40) recombinant viruses containing either wild-type or temperature-sensitive (ts) A mutants of SV40. Cells transformed with the SV40 tsA chimera (HP–A1 and HP–A2), but not the SV40 wild-type chimera (HP–W1), were conditional for

transformation. All three cell lines expressed trophoblast-specific genes, including placental specific genes and the alpha- and beta-subunits of hCG.

These immortalized virus-free human placental cell lines expressing major proteins of human trophoblasts provide efficient *in vitro* models to study placental functions.

Inventor: Janice Y. Chou (NICHD).

Publication: KJ Lei, Y Gluzman, CJ Pan, JY Chou. Immortalization of virus-free human placental cells that express tissue-specific functions. Mol Endocrinol. 1992 May; 6(5):703–712.

Patent Status: HHS Reference No. E–052–2009/0—Research Tool. Patent protection is not being pursued for this technology.

Licensing Status: Available for licensing under a Biological Materials License Agreement.

Licensing Contact: Suryanarayana (Sury) Vepa, PhD, J.D.; 301–435–5020; *vepas@mail.nih.gov*.

Collaborative Research Opportunity: The National Institute of Child Health and Human Development, Section on Cellular Differentiation, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize Immortalized Virus-Free Human Placental Cell Lines. Please contact Joseph Conrad III, PhD at 301–435–3107 or *jmconrad@mail.nih.gov* for more information.

Broadly Applicable Modules for Improved Expression and Detection of Membrane Proteins

Description of Technology: NIH investigators have designed and tested a set of expression modules that are applicable to a wide variety of membrane proteins. Prior to this invention, cloned membrane proteins have sometimes been difficult to detect due to the lack of effective antibodies. Moreover, currently available expression vectors lack the signal sequences, tags, and multiple cloning sites to clone membrane proteins and express them on the cell surface. This invention is the first of its kind to contain all of these elements to facilitate biochemical studies on membrane proteins.

This technology is a set of nucleic acid modules designed for the expression and tagging of membrane proteins in mammalian cells. The module includes a signal peptide, an exchangeable tag, and a multiple cloning site. The gene of a membrane protein may be conveniently inserted into the multiple cloning site, and the signal peptide will target the cloned membrane protein to the cell surface. The tag, in frame with the signal peptide, is either a fluorescent protein or an epitope for a known antibody, both of which enable detection of the protein by several standard biochemical methodologies.

Applications: This technology can provide improved expression and detection of membrane proteins in common laboratory cell lines.

Development Status: Each module contains either one of two different epitope tag, and the expression vector contains either zeocin- or neomycin-resistant markers. There are two sets of module (four vectors) available.

Inventors: Li Lin *et al.* (NIA).

Publication: J Pang, X Zeng, R–P Xiao, EG Lakatta, L Lin. Design, generation, and testing of mammalian expression modules that tag membrane proteins. Protein Science, in press (2009).

Patent Status: U.S. Provisional Application No. 61/142,531 filed 05 Jan 2009 (HHS Reference No. E–016–2009/0–US–01).

Licensing Status: Available for licensing.

Licensing Contact: Fatima Sayyid, MHPM; 301–435–4521; *Fatima.Sayyid@nih.hhs.gov.*

Collaborative Research Opportunity: The National Institute on Aging, Laboratory of Cardiovascular Sciences, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize the technology of mammalian membrane protein expression and detection. Please contact Vio Conley at 301–496–0477 or *conleyv@mail.nih.gov* for more information.

Inhibitors of CD25 To Treat Autoimmune Diseases and Tumors

Description of Technology: This invention discloses therapeutics for the treatment of Multiple Sclerosis, uveitis, and certain cancers by providing methods and compositions for selectively blocking CD25 on T cells or dendritic cells. The therapeutics developed using the current technologies have the potential to exhibit superior specificity and minimal side-effects. In this invention, NIH investigators, for the first time, demonstrate that mature dendritic cells (mDC) use CD25 for trans-presentation of IL–2, and the blockade of CD25 on the surface of mDCs abrogates T cell proliferation. Further, CD25 expression on T cells is not only dispensable for their proliferation, but it also limits effector T cell survival. These observations form the basis for the development of novel therapies for certain cancers and autoimmune disorders.

Applications: Therapeutics for autoimmune diseases; Therapeutics for tumors.

Development Status: Early stage.

Inventors: Bibiana Bielekova *et al.* (NINDS).

Publication: Manuscript submitted for publication.

Patent Status: U.S. Provisional Application No. 61/201,589 filed 12 Dec 2008 (HHS Reference No. E–007–2009/0–US–01).

Licensing Status: Available for licensing.

Licensing Contact: Suryanarayana (Sury) Vepa, PhD, J.D.; 301–435–5020; *vepas@mail.nih.gov*.

Collaborative Research Opportunity: The National Institute of Neurological Disorders and Stoke is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize methods of treating multiple sclerosis by administering agents that block the interaction of dendritic cells and T cells via CD25. Please contact Dr. Martha Lubet at 301–435–3120, e-mail: *lubetm@mail.nih.gov* for more information.

Methods for Identifying Breast Cancer Patients for Therapy With mTOR Inhibitors

Description of Technology: This technology relates to methods of identifying individuals with invasive breast cancer who may benefit from treatment with an inhibitor of mammalian Target of Rapamycin (mTOR), particularly those having a gene amplification including chromosome 8p11–12 or a portion thereof. Chromosome 8p11–12 is the second most commonly amplified region in breast cancer cases, after HER2 amplification at chromosome 17. Similar to HER2 amplification, the amplification of 8p11–12 is associated with decreased survival. However, whereas patients diagnosed with HER2 amplifications can be more effectively treated with adjuvant therapy using HER2 inhibitors such as trastuzumab, no specific therapy has been identified for breast cancer patients having an amplification of chromosome 8p11–12.

Investigators at NIH have shown that amplification of chromosome 8p11–12 leads to increased copy number of the gene for eukaryotic translation initiation factor 4E binding protein 1, or EIF4EBP1 and elevated expression of the protein in these breast cancer cell lines. EIF4E is a rate limiting component of a multi-subunit complex that recruits 40S ribosomal subunits to the 5′ end of

mRNAs. EIF4EBP1 interacts and inhibits EIF4E complex assembly and thus, represses translation. In breast cancer cell lines with EIF4EBP1 amplification, the elevated EIF4EBP1 is largely inactivated via hyperphosphorylation. As the phosphorylation of EIF4EBP1 is controlled by mTOR, its hyperphosphorylation can be reversed with rapamycin. Indeed, rapamycin is much more effective in inhibiting the formation of active translational complex and the growth of breast cancer cells with chromosome 8p11–12/EIF4EBP1 amplification. Thus, detection of chromosome 8p11–12 amplification, and/or over-expression or increased phosphorylation of EIF4EBP1 can be used to identify breast cancer patients for treatment with inhibitors of mTOR, such as rapamycin or its derivatives or analogs.

Applications

- Diagnostic kit for measuring DNA amplification of chromosome 8p11–12 and/or EIF4EBP1 to identify breast cancer patients that could benefit from mTOR inhibitor drugs.
- Diagnostic kit for measuring EIF4EBP1 mRNA or protein levels to help identify breast cancer patients that could benefit from mTOR inhibitor drugs.

Advantages

- This molecular diagnostics may optimize the therapeutic use of mTOR inhibitors in the treatment of breast cancer.
- This molecular diagnostics may stratify breast cancer patients for clinical trials with mTOR targeted agents for increased responses.

Development Status: Early stage; Pre-clinical data available.

Market: Breast cancer is the most common cancer among women in the United States, other than skin cancer. It is the second leading cause of cancer death in women, after lung cancer. An estimated 182,460 new cases of invasive breast cancer were expected to occur among women in the U.S. during 2008. Amplification of chromosome 8p11–12 occurs in about 10–15% of the invasive breast cancer cases.

Inventors: Liang Cao and Paul S. Meltzer (NCI).

Publications: None related to this technology.

Patent Status: U.S. Provisional Application No. 61/152,920 filed 16 Feb 2009 (HHS Reference No. E–340–2008/0–US–01).

Licensing Status: Available for licensing.

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

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

Method for the Diagnosis and Prognosis of Age-Related Cardiovascular Disorders

Description of Technology: NIH investigators have discovered a method for the diagnosis and prognosis of cardiovascular aging. Current methodologies include the measurement of patient lipid profiles or expression of up to two proteins. In contrast, this technology utilizes the expression levels of a panel of proteins not previously known to be related to cardiovascular aging and may prove to be a more accurate diagnostic or prognostic of cardiovascular aging than currently available tests or it may improve the accuracy of currently available tests when used in concert.

The technology relates to methods for determining susceptibility to having an extremely common age-associated vascular disorder. It also describes the subsequent use of these proteins as markers for disease. While the underlying cellular and molecular mechanisms of age-related vascular disease remain largely undefined, the expression levels of the genes described in this technology have been empirically determined to differ between healthy and age-inflamed arterial tissue. Further, this technology includes a companion mass spectroscopic-based methodology for reproducible quantification of specific expression levels of interest.

Application: Diagnosis of age-related vascular disorder.

Development Status: Early stage.

Inventors: Mingyi Wang *et al.* (NIA).

Patent Status: U.S. Provisional Application No. 61/154,329 filed 20 Feb 2009 (HHS Reference No. E–219–2008/0–US–01).

Licensing Status: Available for licensing.

Licensing Contact: Fatima Sayyid, MHPM; 301–435–4521; *Fatima.Sayyid@nih.hhs.gov.*

Collaborative Research Opportunity: The National Institute on Aging, Cardiovascular Biology Unit-Vascular Group, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize idea of how to assess and retard accelerated arterial aging and its attendant risks for atherosclerosis and hypertension. Please contact Vio Conley at 301–496–0477 or *conleyv@mail.nih.gov* for more information.

CCR5-Specific Human Monoclonal Antibodies

Description of Technology: The subject invention describes the anti-CCR5 monoclonal antibodies, their fusion protein, conjugates, derivatives, or fragments, DNA sequences encoding such antibodies, host cells containing such DNA sequences, as well as the methods to produce them recombinantly and their pharmacological composition.

It has been demonstrated that the HIV co-receptor CCR5 plays an important role in virus entry. The subject antibodies exhibited neutralization activity against HIV–1 infection by binding to cell associated CCR5 in vitro. Therefore, subject anti-CCR5 antibodies can be useful research materials for the research in HIV/AIDS fields.

Applications: Research tools.

Development Status: In vitro data is available at this time.

Inventors: Dimiter S. Dimitrov and Mei-Yun Zhang (NCI).

Related Publications

1. C Pastori *et al.* Long-lasting CCR5 internalization by antibodies in a subset of long-term nonprogressors: a possible protective effect against disease progression. Blood. 2006 Jun 15;107(12):4825–4833.

2. MY Zhang, B Vu, CC Huang, I Sidirov, V Choudhly, PD Kwong, DS Dimitrov. Identification of human monoclonal antibodies specific for CCR5 from an antibody library derived from HIV-infected long-term non-progressors. Retrovirology. 2006 Dec 21;3 Suppl 1:S61.

3. DS Dimitrov. Virus entry: molecular mechanisms and biomedical applications. Nat Rev Microbiol. 2004 Feb;2(2):109–122.

Patent Status: HHS Reference No. E–297–2006/0—Research Tool. Patent protection is not being pursued for this technology.

Licensing Status: Available for licensing.

Licensing Contact: Sally Hu, PhD; 301–435–5606; *HuS@mail.nih.gov.*

Dated: May 27, 2009.

Richard U. Rodriguez,

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

[FR Doc. E9–12873 Filed 6–2–09; 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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Diagnostic Markers for Melanoma

Description of Technology: This invention relates to diagnostic and prognostic markers for melanoma. It discloses the identification of somatic mutations in genes of the microphthalmia-associated transcription factor (MITF) pathway in patients with melanoma.

Melanoma is an aggressive and often fatal cancer with increasing incidence worldwide. Previous studies have linked the MITF pathway to the progression of melanoma. However, little is known about somatic mutations in genes of the MITF pathway that contribute to the development and progression of melanoma. To assess the role of the MITF pathway in melanoma, NIH investigators evaluated primary and metastatic melanoma samples for the presence of somatic mutations in two genes of the MITF pathway, MITF and SRY (sex determining region Y)—box 10 (SOX10). They identified 16 previously unidentified somatic mutations in these genes. These studies suggest that MITF and SOX10 genes be used as diagnostic markers in human metastatic melanoma.

Applications

• Diagnosis and prognosis of patients with melanoma by detecting any mutations in the MITF or SOX10 gene.

• Selection of therapy for melanoma patient; an MITF inhibitor can be selected for therapy if the patient has any of the disclosed mutations in MITF.

Market: Cancer is the second leading cause of death in the U.S. There is an acute need for cancer biomarkers that can be detected from clinically relevant samples and used for early diagnosis, therapeutic follow-up and prognosis of malignant diseases. Melanoma is the most serious type of cancer of the skin. The percentage of people who develop melanoma has more than doubled in the past 30 years. There are 68,720 estimated new cases and 8,650 estimated deaths from melanoma in the United States in 2009, according to the National Cancer Institute.

Inventors: Yardena R. Samuels *et al.* (NHGRI).

Publication: Cronin JC WJ, Loftus SK, Prickett TD, Wei X, Ridd, Vemula S, Burrell AS, Agrawal NS, Lin JC, Banister CE, Buckhaults P, Rosenberg SA, Bastian BC, Pavan WJ, Samuels Y: Frequent mutations in the MITF pathway in melanoma. Pigment Cell and Melanoma Research 2009, (In Press).

Patent Status: U.S. Provisional Application No. 61/214,415 filed 22 Apr 2009 (HHS Reference No. E–053–2009/0–US–01).

Licensing Status: Available for licensing.

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

Collaborative Research Opportunity: The National Human Genome Research Institute's Cancer Genetics Branch is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize these newly identified candidate melanoma diagnostic and prognostic markers. Please contact NHGRI's Technology Development Coordinator (TDC) Claire T. Driscoll at *cdriscol@mail.nih.gov* for more information.

T Cells Attacking Cancer: T Cell Receptors That Recognize the Tyrosinase Tumor Antigen

Description of Technology: A problem with current chemotherapy-based cancer treatments is the harsh side-effects associated with many cancer drugs. Thus, there is an urgent need to develop new therapeutic strategies combining fewer side-effects and more specific anti-tumor activity. Adoptive cell transfer (ACT) is a promising new immunotherapeutic approach to treat cancer and other diseases by directing an individual's innate and adaptive immune system to recognize specific disease-associated antigens.

T cell receptors (TCRs) are proteins that recognize antigens in the context of infected or transformed cells and activate T cells to mediate an immune response and destroy abnormal cells. TCRs consist of two domains, one variable domain that recognizes the antigen and one constant region that helps the TCR anchor to the membrane and transmit recognition signals by interacting with other proteins.

Scientists at the National Institutes of Health (NIH) have isolated T cells that recognize the human tyrosinase tumor-associated antigen (TAA) from the tumor infiltrating lymphocytes (TIL) of a melanoma cancer patient. The human tyrosinase antigen is a tumor antigen expressed in a variety of cancers, including skin cancer (melanoma) and brain cancer (glioblastoma). Utilizing the tyrosinase specific T cells, these scientists developed human/mouse hybrid TCRs with enhanced affinity for the tyrosinase TAA. The TCR sequences were modified by making specific amino acid substitutions and replacing certain TCR regions with mouse homologues. These TCRs also showed CD8-independency and, thus, can be expressed in both CD8 and CD4 T cells. T cells expressing these engineered TCRs recognize skin and brain tumor cells in culture. These T cells also exhibit enhanced cytokine induction and better tumor reactivity compared to unmodified TCRs. Previous versions of gene-modified T cells developed by NIH researchers demonstrated objective clinical responses in some cancer patients, which have validated gene-modified T cell immunotherapy as a promising cancer treatment strategy. TCRs directed against the tyrosinase TAA could serve as valuable new immunotherapeutic tools for attacking tumors, especially in patients whose tumors do not express other common TAAs.

Applications

• Immunotherapeutics to treat and/or prevent the recurrence of a variety of human cancers, including melanomas and glioblastomas, that express tyrosinase by transferring T cells engineered with tyrosinase-specific TCRs into cancer patients.