billion by 2012 according to some reports.

Overall, the potential commercial opportunity based on the subject technology is immense.

Inventors: Bernard Moss *et al.* (NIAID).

Publications: The inventor, Dr. Bernard Moss, is an author of more than 100 publications in the area covered by the subject patents. The following is just a sampling of his publications in the area:

1. B Moss and PL Earl. Overview of the vaccinia virus expression system. Curr Protoc Mol Biol. 2002 Nov; Chapter 16: Unit16.15.
2. HL Robinson, S Sharma, J Zhao, S Kannanganat, L Lai, L Chennareddi, T Yu, DC Montefiori, RR Amara, LS Wyatt, B Moss. Immunogenicity in macaques of the clinical product for a clade B DNA/MVA HIV vaccine: elicitation of IFN-gamma, IL–2, and TNF-alpha coproducing CD4 and CD8 T cells. AIDS Res Hum Retroviruses. 2007 Dec;23(12):1555–1562.
3. LS Wyatt, PL Earl, J Vogt, LA Eller, D Chandran, J Liu, HL Robinson, B Moss. Correlation of immunogenicities and in vitro expression levels of recombinant modified vaccinia virus Ankara HIV vaccines. Vaccine 2008 Jan 24;26(4):486–493.
4. M Hebben, J Brants, C Birck, JP Samama, B Wasylyk, D Spehner, K Pradeau, A Domi, B Moss, P Schultz, R Drillien. High level protein expression in mammalian cells using a safe viral vector: modified vaccinia virus Ankara. Protein Expr Purif. 2007 Dec;56(2):269–278.

Patent Status: The technology is described and claimed in the following four (4) patents that were issued in the U.S. in 2006 (HHS Reference E–552–1982/2):

1. USPN 6,998,252 issued February 14, 2006, ''Recombinant Poxviruses Having Foreign DNA Expressed under the Control of Poxvirus Regulatory Sequences''.
2. USPN 7,015,024 issued March 21, 2006, ''Compositions Containing Recombinant Poxviruses Having Foreign DNA Expressed Under the Control of Poxvirus Regulatory Sequences''.
3. USPN 7,045,313 issued May 16, 2006, ''Recombinant Vaccinia Virus Containing Chimeric Gene Having Foreign DNA Flanked by Vaccinia Regulatory DNA''.
4. USPN 7,045,136 issued May 16, 2006, ''Methods of Immunization Using Recombinant Poxviruses Having Foreign DNA Expressed Under the Control of Poxvirus Regulatory Sequences''.

Licensing Status: Available for licensing.

Licensing Contacts: Uri Reichman, Ph.D., MBA; 301–435–4616; *ur7a@nih.gov*; RC Tang, JD, LLM; 301–435–5031; *tangrc@mail.nih.gov*.

Dated: August 10, 2009.

Richard U. Rodriguez,

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

[FR Doc. E9–19693 Filed 8–14–09; 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.

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.

Superior Method of Preparing Dendrimers for Use as Magnetic Resonance Imaging (MRI) Contrast Agents

Description of Technology: There is a need to develop more efficient gadolinium-containing (Gd) contrast agents for magnetic resonance imaging (MRI) as the small molecules presently used clinically have the disadvantage of being rapidly cleared from circulation and excreted by the kidneys.

Dendrimer-based macromolecular MRI contrast agents in which numerous chelated Gd ions are covalently attached to a multivalent dendritic architecture are a promising class of diagnostic agents for medical imaging applications. Clinical development of the dendrimer-based agents has been limited as the current methods for synthesizing them result in a complex mixture that produces inconsistent imaging results.

The present technology describes the development of a new method of pre-forming the metal-ligand chelate in alcohol prior to conjugation to the dendrimer. Specifically, for example, a 1B4M–DTPA–Gd chelate is preformed in methanol and purified prior to conjugation to a PAMAM dendrimer molecule. This results in a dendrimer-based MRI contrast agent with greatly improved homogeneity and stability, and possessing an unexpectedly greater molar relaxivity that allows the use of much less of the agent than previously required to obtain comparable images. The use of a DOTA–Gd chelate is equally possible.

Application: An improved method for synthesis of dendrimer-based MRI contrast agents that is greatly suited for clinical development.

Advantages

- Efficient preparation of stable dendrimer-based contrast agents suitable for medical imaging.
- Higher molar relaxivity translates into a lower dosage needed for imaging.
- Ability to control dendrimer size conducive for development of compartment-specific imaging agents.

Market: Dendrimers show particular promise for the development of cancer imaging agents. The ability to exquisitely control dendrimer size enables delivering them to specific compartments such as small tumors allowing for early cancer detection. Gadolinium (Gd) chelates are extensively used as MRI contrast agents and have proven to be safe. The combination of gadolinium chelates with dendrimer chemistry could greatly enhance the versatility of MRI imaging.

Inventors: Kido Nwe and Martin W. Brechbiel (NCI).

Publications

1. K Nwe, H Xu, CA Regino, M Bernardo, L Ileva, L Riffle, KJ Wong, MW Brechbiel. A new approach in the preparation of dendrimer-based bifunctional diethylenetriaminepentaacetic acid MR contrast agent derivatives. Bioconjugate Chem. 2009 Jul;20(7):1412–1418.
2. OA Gansow, MW Brechbiel, MA Magerstadt. Complexes of functionalized tetraazacyclododecane chelates with bismuth, lead, yttrium, actinium, or lanthanide metal ions. U.S. Patent 5,428,154 issued 27 Jun 1995.

Patent Status: U.S. Provisional Application No. 61/180,327 filed 21 May 2009 (HHS Reference No. E–207–2009/0–US–01).

Related Technology: OA Gansow, MW Brechbiel, MA Magerstadt, ''Complexes of Functionalized Tetraazacyclododecane Chelates with Bismuth, Lead, Yttrium, Actinium, or

Lanthanide Metal Ions,'' U.S. Patent 5,428,154 issued 27 Jun 1995 (HHS Reference No. E–347–1996/0–US–22).

Licensing Status: Available for licensing.

Licensing Contact: Sabarni Chatterjee, Ph.D.; 301–435–5587; *chatterjeesa@mail.nih.gov*.

Collaborative Research Opportunity: The Inorganic & Radioimmune Chemistry Section, ROB, CCR, NCI is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize macromolecular (dendrimer-based) MR contrast agents as well as multi-modality analogs. Please contact John D. Hewes, Ph.D. at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Two Types of Dentin Sialophosphoprotein (DSPP) Knockout Mice

Description of Technology: Two types of dentin sialophosphoprotein knockout mice are available for licensing. The technology relates to two separate knockout mouse models of the role of dentin sialophosphoprotein in dentin mineralization and development of teeth. The first knockout mouse is a knockout of the entire DSPP gene, which results in a phenotype similar to human autosomal dominant dentinogenesis imperfecta, in which teeth have widened predentin and irregular dentin mineralization resulting in sporadic unmineralized areas in dentin and frequent pulp exposures. DSPP protein in odontoblasts is normally proteolytically cleaved into two products, dentin sialoprotein (DSP) and dentin phosphoprotein (DPP). To distinguish the role of the proteolytic fragments, the second knockout mouse (DPPcKO) consists of a transgene expressing the DSP fragment in a DSPP null background. The DPPcKO mouse demonstrates a partial rescue of the DSPP knockout effect and indicates DSP and PPP have distinct roles in dentin development.

Applications

- Tool for studying dentin development.
- Tool for developing treatments for autosomal dominant dentinogenesis imperfecta.

Inventors: Ashok Kulkarni and Shigeki Suzuki (NIDCR)

Related Publications

1. Sreenath T, Thyagarajan T, Hall B, Longenecker G, D'Souza R, Hong S, Wright JT, MacDougall M, Sauk J, Kulkarni AB. Dentin sialophosphoprotein knockout mouse teeth display widened predentin zone and develop defective dentin mineralization similar to human dentinogenesis imperfecta type III. J Biol Chem. 2003 Jul 4;278(27):24874–24880.
2. Suzuki S, Sreenath T, Haruyama N, Honeycutt C, Terse A, Cho A, Kohler T, Muller R, Goldberg M, Kulkarni A. Dentin sialoprotein and dentin phosphoprotein have distinct roles in dentin mineralization. Submitted, 2009.

Patent Status: HHS Reference No. E–201–2009/0—Research Tool. Patent protection is not being pursued for this technology.

Licensing Status: This technology is available as a research tool under a Biological Materials License.

Licensing Contact: Steve Standley, PhD; 301–435–4074; *sstand@od.nih.gov*.

Novel Diagnostic and Therapeutic Biomarkers for Squamous Cell Carcinomas

Description of Technology: Head and neck squamous cell carcinoma (HNSCC) includes tumors of the nasal cavities, paranasal sinuses, oral cavity, nasopharynx, oropharynx, hypopharynx, and larynx. HNSCC is an aggressive cancer with poor prognosis after metastasis. In patients where HNSCC is identified early, prognosis is better and patient survival increases. However, at present, very few if any biomarkers are available to diagnosis HNSCC. The overall 5-year survival rate for patients is only 50% and has not improved in over 30 years. New treatments and diagnostics for early detection are needed to improve patient survival and quality of life for this these types of cancers.

Scientists at the National Institutes of Health (NIH) have discovered that the TGF-β signaling pathway crosstalks with the PI3K/Akt signaling pathway to suppress squamous cell carcinomas (SCCs). When the TGF-β pathway is inactivated and the PI3K pathway becomes hyperactive, HNSCC development is accelerated. Combined mutations in the transforming growth factor-β receptor type 1 (TGFβR1) gene and the phosphate and tensin homolog (PTEN) gene directly correlate with an individual having HNSCC or being increasingly susceptible to HNSCC. When tumor-associated mutations in both biomarkers were induced in animal subjects, spontaneous SCCs were developed in every test subject. Given this high correlation, this technology could be utilized to improve diagnosis of HNSCC at its early stages when the malignancy is most treatable. This technology also includes therapeutic combinations of TGF-β and PI3K/Akt modulators as treatments for HNSCC and methods of treating patients diagnosed with HNSCC.

Applications

- Biomarkers to diagnose patients with HNSCC or predict patients who have a high susceptibility for developing HNSCC.
- Diagnostic tool to identify patients predicted to respond to specific HNSCC therapies as part of a personalized treatment strategy.
- Therapeutic drug combinations of TGF-β pathway modulators and PI3K/Akt inhibitors to treat various head and neck cancers, including nasal, oral, pharyngeal, laryngeal, and cranial tumors.

Advantages

- Complete Penetrance: All test subjects exhibiting mutations in the TGFβR1 and PTEN genes develop HNSCC. A diagnostic kit that includes assays for these mutations is predicted to have high accuracy for identifying HNSCC.
- Earlier diagnosis could yield more effective treatments: This technology could provide for a more accurate and earlier diagnosis of SCCs to revolutionize the treatment of this malignancy. Current SCC therapies may become more effective treatments and new therapies could be developed as better treatment options.
- Diagnostic for HNSCC susceptibility could lead to HNSCC prevention: This technology could identify patients predisposed to developing HNSCC in order to help prevent individuals from developing head and neck cancer.

Development Status: This technology is in the pre-clinical stage of development. *In vivo* and *in vitro* mouse data is available.

Market: Cancer continues to be a medical and financial burden on U.S. public health. The incidence of HNSCC is over 500,000 cases worldwide and approximately 47,000 new cases are diagnosed each year in the United States. Despite our increasing knowledge of cancer treatment and diagnosis methods, the fight against cancer will continue to benefit from the development of new technologies aimed at treating individuals with disease and diagnosing susceptible patients.

Inventors: Ashok B. Kulkarni and Yansong Bian (NIDCR).

Publications

1. Y Bian *et al.* Progressive tumor formation in mice with conditional deletion of TGF-β signaling in head and neck epithelia is associated with activation of the PI3k/Akt Pathway. Manuscript in preparation (accepted).

2. Y Honjo *et al.* TGF-beta receptor I conditional knockout mice develop spontaneous squamous cell carcinoma. Cell Cycle 2007 Jun 1:6(11):1360–1366.

Patent Status: U.S. Provisional Application No. 61/176,723 filed 08 May 2009 (HHS Reference No. E–118–2009/0–US–01).

Licensing Status: Available for licensing.

Licensing Contact: Samuel E. Bish, Ph.D.; 301–435–5282; *bishse@mail.nih.gov*.

Antigen Mixtures for Serological Detection of HHV–8 Infection

Description of Technology: This invention describes a highly specific and sensitive serological test for human herpesvirus 8 (HHV–8) infection that uses the Luciferase Immunoprecipitation System (LIPS). A mixture of four virus-specific antigens, including K8.1, v-cyclin, ORF65 and LANA, was shown to provide more robust detection of HHV–8 infection than traditional methods due its ability to detect very low viral loads. In addition, one of the antigens, v-cyclin, was identified as a new serological marker for HHV–8 infection, and its similarity to a known human oncogene, cyclin-D, raises the possibility of its use as a diagnostic tool for detecting cancer.

This test is more sensitive and amenable to a high-throughput format than other conventional tests for HHV–8 infection such as Immunofluorescent Assays, Western Blots, ELISAs and PCR based approaches. It simplifies data collection and analysis and allows for more rapid clinical output. Validation tests on patient sera samples using this 4-antigen mixture has shown 100% sensitivity and specificity compared to 94% for ELISAs.

The test can be incorporated into routine screening panels for rapid screening of HHV–8 infection, and may be potentially adapted for use as a diagnostic tool for detecting cancer. A successful embodiment of the test can be incorporated into routine blood screening panels, and may lead a reduced risk of transfusion-transmitted HHV–8 infection in patients. It may also be useful for detecting HHV–8 induced cancer in HIV infected patients.

Applications

- Rapid and efficient serological screening of HHV–8 infection.
- Cancer diagnostics.

Development Status: Early Stage.

Inventors: Peter D. Burbelo (NIDCR), Joseph A. Kovacs (CC), Michael J. Iadarola (NIDCR).

Publication: PD Burbelo, HP Leahy, S Groot, LR Bishop, W Miley, MJ Iadarola, D Whitby, JA Kovacs. Four-antigen mixture containing v-cyclin for serological screening of human herpesvirus 8 infection. Clin Vaccine Immunol. 2009 May;16(5):621–627.

Patent Status: U.S. Patent Application No. 61/152,058 filed 12 Feb 2009 (HHS Reference No. E–063–2009/0–US–01).

Licensing Status: Available for licensing.

Licensing Contact: Jeffrey A. James, PhD; 301–435–5474; *jeffreyja@mail.nih.gov*.

Oligo Microarray for Detection of All Known Mammalian and Avian Pathogenic Viruses

Description of Technology: The spectrum of pathogenic viruses of importance in human disease, agriculture and biology is not only large and diverse, but continually evolving. The identification or isolation of viral pathogens, in correlation with the presence of specific disease phenotypes, is of paramount importance both to diagnosis of disease and the subsequent management or treatment of viral infection. The limitations of current viral detection methods, such as PCR and immunoassays, led to the development of a novel microarray system for specific detection of viruses. The technology offered here for licensing provides a method for high-throughput screening of known pathogenic viruses along with identification of ''new'' disease-associated viruses.

The novel method is based on a viral microarray containing 10,000 immobilized DNA oligonucleotide features, representing all known mammalian and avian pathogenic viruses (approximately 600). Software was also developed to analyze the viral microarray results. The oligonucleotide features in this system are 60-mer long and distributed across both conserved and non-conserved regions of known viral sequences. This design serves the dual purpose of: (1) Facilitating validation via redundant signals associated with each represented virus and (2) allowing for the discovery of new viruses, which arise due to recombination. In addition, positive and negative controls against human and mouse housekeeping genes are included along with software for analysis of virus microarray results.

Further advantages of the viral microarray include: (a) The use of sample inputs as little as 10ng of either total DNA or RNA extracted from virus infected cells, representing as few as 20 viral particles; (b) detection of viruses of both DNA and RNA classes; (c) a capacity for high-throughput screening of various sample types including serum, saliva and biopsy tissues; and (d) analysis of a large number of samples in parallel on identical arrays.

The detection of viral DNA is unique to this technology, as other available technologies only detect viral genomic RNA or viral mRNA transcripts. Additionally, the viral chip was found to be highly specific and sensitive for detecting different viral genomic sequences in cell lines and multiple viral constructs co-infection in cultured cells.

Applications

- Detection and identification of viruses that cause disease.
- Efficient discovery of new pathogenic viruses.
- Diagnosis of human and animal disease outbreaks.
- Identification of viral agents used in bioterrorism.

Development Status

- The pre-clinical performance of the viral microarray was evaluated by application of four virally positive infected cell lines (JSC–1-harboring EBV and KSHV, BCBL–1 harboring KSHV, HeLa- harboring HPV18, Cem X 174 harboring SIV).
- Clinical performance was tested and validated through analysis of total RNA from cold (swab), Japanese Encephalitis, Dengue, Ebola and West Nile virus samples.

Inventors: Cassio S Baptista and David J Munroe (NCI).

Patent Status: U.S. Patent Application No. 11/800,080 filed 02 May 2007 (HHS Reference No. E–206–2006/0–US–03).

Licensing Status: Available for licensing.

Licensing Contact: Jeffrey A. James Ph.D.; 301–435–5474; *jeffreyja@mail.nih.gov*.

Collaborative Research Opportunity: The NCI Laboratory of Molecular Technology is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this oligo microarray for identification and detection of all known mammalian and avian pathogenic viruses. Please contact John D. Hewes, PhD at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Dated: August 10, 2009.

Richard U. Rodriguez,

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

[FR Doc. E9–19691 Filed 8–14–09; 8:45 am]

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