expression is significantly increased in the brain of PD patients, while expression of miR–205 is specifically down-regulated in the same patients. Also, the NIH inventors have discovered that the expression levels of LRRK2 and miR–205 are dynamically regulated and reversely correlated in multiple brain regions and at different ages in mouse brains, indicating that miR–205 plays a regulatory role in LRRK2 protein expression.

Based on these novel findings, the present technology provides for novel methods of treatment of patients suffering from PD disease by modulating the amount of miR–205 in patients by administration of a miR–205 gene product, a vector encoding a miR–205 gene product or an agent that increases expression of miR–205. The present technology also provides for methods of determining the effectiveness of different candidate drugs for the treatment of PD, methods of diagnosing PD, or having an increased susceptibility to developing PD, and an *in vitro* process for identifying a therapeutic agent for the treatment of PD.

Applications: Therapeutics and diagnostics for PD.

Development Status: Early-stage.

Inventors: Huaibin Cai and Hyun J. Cho (NIA).

Patent Status: U.S. Provisional Application No. 61/430,626 filed 07 Jan 2011 (HHS Reference No. E–209–2010/0–US–01).

Licensing Status: Available for licensing.

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

Collaborative Research Opportunity: The National Institute on Aging, Transgenics Section, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize microRNA–205 or other reagents for the treatment and diagnosis of Parkinson Disease. Please contact Nicole Guyton, PhD at 301–435–3101 or *darackn@mail.nih.gov* for more information.

Dated: June 14, 2011.

Richard U. Rodriguez,

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

[FR Doc. 2011–15467 Filed 6–21–11; 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.

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.

Monoclonal Antibodies to Glypican-3 Protein and Heparin Sulfate for Treatment of Cancer

Description of Technology: Hepatocellular carcinoma (HCC) is the most common form of liver cancer, and is among the more deadly cancers in the world due to its late detection and poor prognosis. HCC is often associated with liver disease, curtailing traditional chemotherapy as a treatment option. While surgical resection offers the best method for long term treatment of the disease, only a small portion of HCC patients are eligible for this procedure. As a result, there is a need for new treatments that can be successfully applied to a large population of HCC patients.

Glypican-3 (GPC3) is a cell surface protein that is preferentially expressed on HCC cells. Evidence has demonstrated that a soluble form of GPC3 that is incapable of cell signaling has the ability to inhibit the growth of HCC cells. This suggested that blocking GPC3 signaling could serve as a therapeutic approach for treating HCC.

This invention concerns monoclonal antibodies against GPC3 and their use, either by themselves or as the targeting domain for an immunotoxin, for the treatment of GPC3-expressing cancers such as HCC. Specifically, the inventors have generated two distinct monoclonal antibodies to GPC3. The first monoclonal antibody (HN3) binds to a conformational epitope on the cell surface domain of GPC3. The second monoclonal antibody (HS20) binds specifically to heparin sulfate chains on GPC3.

By blocking GPC3 function, these antibodies can inhibit the growth of HCC cells, thereby decreasing the ability of tumors to grow and metastasize. Furthermore, by using the antibodies to target a toxin to only those cells that express GPC3, cancer cells can be eliminated while allowing healthy, essential cells to remain unharmed. Thus, monoclonal antibodies to GPC3 (and corresponding immunotoxins) represent a novel therapeutic candidate for treatment of HCC, as well as other cancers associated with the differential expression of GPC3.

Applications:

- Therapeutic candidates against cancers that overexpress GPC3;
- Antibodies for killing cancer cells by inhibiting GPC3-based cell signaling, thereby inhibiting tumor cell growth;
- Immunotoxins for killing cancer cells through the action of a toxic agent;
- Diagnostics for detecting cancers associated with GPC3 overexpression;
- Specific cancers include hepatocellular cancer (HCC), melanoma, thyroid cancer, lung squamous cell carcinoma, Wilms' tumor, neuroblastoma, hepatoblastoma, and testicular germ-cell tumors.

Advantages:

- Monoclonal antibodies create a level of specificity that can reduce deleterious side-effects;
- Multiple treatment strategies available including the killing of cancer cells with a toxic agent or by inhibiting cell signaling;
- Non-invasive and potentially non-liver toxic alternative to current HCC treatment strategies.

Development Status: Preclinical stage of development; cell culture data with HCC cells.

Inventors: Mitchell Ho (NCI) *et al.*

Patent Status: U.S. provisional application 61/477,020 (HHS technology reference E–130–2011/0–US–01).

For more information, see:

- M Feng *et al.* Recombinant soluble glypican 3 protein inhibits the growth of hepatocellular carcinoma *in vitro.* Int J Cancer 2011 May1;128(9):2246–2247, doi 10.1002/ijc.25549. [PMID: 20617511].
- SI Zitterman *et al.* Soluble glypican 3 inhibits the growth of hepatocellular

carcinoma *in vitro* and *in vivo.* Int J Cancer 2010 Mar 15;126(6):1291–1301. [PMID: 19816934].

Licensing Status: Available for licensing.

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

Collaborative Research Opportunity: The Center for Cancer Research, Laboratory of Molecular Biology, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize human monoclonal antibodies or immunoconjugates such as immunotoxins and antibody-drug conjugates against GPC3, soluble GPC3 and its immunoconjugates such as Fc fusion proteins, large scale antibody production, and HCC xenograft mouse models. Please contact John Hewes, PhD at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Mouse Xenograft Model for Mesothelioma

Description of Technology: Malignant mesothelioma is a cancer that presents itself in the protective lining of several organs (*e.g.,* lung, heart, testis, etc.). The primary cause for mesothelioma is direct or indirect exposure to asbestos, although the disease can present without any prior exposure. Mesothelioma is relatively rare, but the prognosis for patients is poor, indicating a need to better understand and treat the disease. Current treatments often involve chemotherapy and radiation therapy, although recent studies have employed the use of therapeutic antibodies and antibody-targeted toxins.

This invention involves the creation of a new mouse model for mesothelioma. By creating xenografts with mesothelioma cells that express GFP-Luciferase fusion proteins, the xenografts can be detected to a high degree of sensitivity, and monitored for several months following implantation. The high level of detection sensitivity improves the ability to monitor disease progression in response to therapeutic candidates, thereby allowing more efficient drug screening and evaluation. This has already been demonstrated by using the mouse to evaluate an anti-mesothelioma immunotoxin known as SS1P, a drug candidate that is currently being evaluated for clinical effectiveness.

Applications:

- Animal model for screening compounds as potential therapeutics for mesothelioma;
- Animal model for studying the effectiveness of potential therapeutics for mesothelioma;
- Animal model for studying the pathology of mesothelioma.

Advantages:

- The model is created using well characterized, art-accepted mesothelioma cells;
- The model exhibits the classical clinical progression of mesothelioma, demonstrating its accuracy as a model;
- The use of GFP-Luciferase fusion proteins allow for non-invasive evaluation of mesothelioma progression and response to drug candidates;
- The use of GFP-Luciferase fusion proteins allow the use of highly sensitive detection systems such as bioluminescence.

Benefits:

- The convenient and efficient identification and evaluation of mesothelioma drug candidates.

Inventor: Mitchell Ho (NCI).

Patent Status: HHS Reference No. E–302–2009/0 — Research Tool. Patent protection is not being pursued for this technology.

For more information, see:

- M. Feng *et al.* In vivo imaging of human malignant mesothelioma grown orthotopically in the peritoneal cavity of nude mice. J Cancer. 2011 Mar 1;2:123–131. [PMID: 21479131];
- PCT Patent Application WO 2010/065044 (HHS technology reference E–336–2008/0–PCT–02);
- U.S. Patent 7,081,518 (HHS technology reference E–139–1999/0–US–07).

Licensing Status: The technology is available for non-exclusive licensing as a Biological material/Research tool.

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

Collaborative Research Opportunity: The Center for Cancer Research, Laboratory of Molecular Biology, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize monoclonal antibodies and immunoconjugates targeting malignant mesotheliomas. Please contact John Hewes, PhD at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

Increased Therapeutic Effectiveness of Immunotoxins Through the Use of Less Immunogenic Toxin Domains

Description of Technology: Targeted toxins (*e.g.,* immunotoxins) are therapeutics that have at least two important components: (1) A toxin domain that is capable of killing cells and (2) a targeting domain that is capable of selectively localizing the toxic domain to only those cells which should be killed. By selecting a targeting domain that binds only to certain diseased cells (*e.g.,* a cell which only expresses a cell surface receptor when in a diseased state), targeted toxins can kill the diseased cells while allowing healthy, essential cells to survive. As a result, patients receiving a targeted toxin are less likely to experience the deleterious side-effects associated with non-discriminate therapies such as chemotherapy or radiation therapy.

A particular toxin that has been used in targeted toxins is *Pseudomonas* exotoxin A (PE). The effectiveness of PE-containing targeted toxins has been demonstrated against various forms of cancer, including hairy cell leukemia (HCL) and pediatric acute lymphocytic leukemia (pALL). Although early variations these targeted toxins have demonstrated efficacy upon first administration, the continued administration of a targeted toxin often leads to a reduced patient response. The primary cause of the reduced response is the formation of neutralizing antibodies against PE by the patient.

Several variations of PE have been created to reduce the immunogenicity of PE as a means of increasing the therapeutic effectiveness of targeted toxins through multiple rounds of drug administration. This technology involves the identification of two important B-cell epitopes on PE, and the elimination of those epitopes by mutation. These new PE variants retain a sufficient cell killing activity while increasing their therapeutic effectiveness toward patients that receive multiple administrations. By further combining these new mutations with previously identified modifications that also improve the efficacy of PE-based targeted toxins, it may be possible to treat any disease characterized by cells that express a particular cell surface receptor when in a disease state.

Applications:

- Essential component of a targeted toxin, such as an immunotoxin (antibody-targeted toxin) or ligand-targeted toxin;
- Treatment of diseases that are associated with the increased expression of a cell surface receptor;
- Applicable to any disease associated with cells that preferentially express a specific cell surface receptor;
- Relevant diseases include various cancers, including lung, ovarian, breast, head and neck, and hematological cancers.

Advantages:

• Less immunogenic targeted toxin results in improved efficacy during multiple administrations;

• Targeted therapy decreases non-specific killing of healthy, essential cells, resulting in fewer side-effects and healthier patients.

Development Status: Preclinical stage of development.

Inventors: Pastan (NCI) *et al.*

Patent Status:

• U.S. provisional application 61/241,620 (HHS technology reference E–269–2009/0–US–01);

• PCT patent application PCT/US2010/048504 (HHS technology reference E–269–2009/0–PCT–02).

For more information, see:

• U.S. Patent Publication US 20100215656 A1 (HHS technology reference E–292–2007/0–US–06);

• U.S. Patent Publication US 20090142341 A1 (HHS technology reference E–262–2005/0–US–06);

• U.S. Patent 7,777,019 (HHS technology reference E–129–2001/0–US–07).

Licensing Status: Available for licensing.

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

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

Dated: June 15, 2011.

Richard U. Rodriguez,

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

[FR Doc. 2011–15492 Filed 6–21–11; 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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Mouse Model for Cerebral Cavernous Malformation, an Inherited Brain Disorder

Description of Technology: Cerebral Cavernous Malformation (CCM) is a brain disease affecting up to 0.5% of the worldwide population. CCM is characterized by grossly dilated vessels prone to leaking and hemorrhage which result in severe headaches, seizures, and strokes. Inherited forms of the disease are due to mutations in one of three loci, CCM1, CCM2, and CCM3. Prior efforts to develop mice with targeted null mutations in *Ccm1, Ccm2,* or *Ccm3* have been unsuccessful, as such mutations result in embryonic death.

The inventors have developed the first mouse model available for the study of CCM, in which mouse *Ccm2* can be conditionally deleted in blood-accessible and endothelial cells, resulting in neurological defects, ataxia, and brain hemorrhages consistent with the human disease. The model was generated through a cross of C57BL/6 *Ccm2*-floxed mice with C57BL/6 *MX–1–Cre* mice, which permits inducible ablation by polyinosinic:polycytidylic acid (pIpC).

Inventors: Ulrich Siebenlist (NIAID) and Yoh-suke Mukoyama (NHLBI).

Related Publications: In preparation.

Patent Status: HHS Reference No. E–158–2011/0—Research Material. Patent protection is not being pursued for this technology.

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

Licensing Contact: Tara L. Kirby, PhD; 301–435–4426; *tarak@mail.nih.gov.*

System to Increase Consistency and Reduce Variations in Contrast and Sensitivity in MRI Imaging

Description of Technology: The technology relates to the field of MRI. More specifically, the invention describes and claims system and methods related to the use of non-linear B_0 shims to improve excitation flip angle uniformity in high field MRI. The disclosed system and methods can be used in conjunction with existing multi-dimension excitation methods, including those that use parallel excitation to improve contrast and sensitivity in gradient echo magnetic resonance imaging. The technology is designed to overcome shortcomings associated with high field MRI, namely RF flip angle inhomogeneity due to wavelength effects that can lead to spatial variations in contrast and sensitivity.

Applications: High field MRI.

Advantages: The present system and methods will improve performance of high field MRI:

• Improve the transmit profile homogeneity, and therefore the uniformity of MRI images.

• The method is applicable to all MRI scanning with poor B1 uniformity. This includes situations when B1 variations are caused by the coil B1 profile, by the dielectric properties of the object (wavelength effects), or by a combination of both.

• The method is applicable with currently available single or multi-channel B1 coils.

Development Status:

• Proof of principle has been demonstrated on a prototype device.

• Demonstration of the application to human imaging is currently underway.

Inventors: Jeff Duyn (NINDS).

Relevant Publication: Duan Q, van Gelderen P, Duyn J. B_0 based shimming of RF flip angle in MRI. Submitted to Magnetic Resonance in Medicine.

Patent Status: U.S. Provisional Application No. 61/473,610 filed 08 Apr 2011 (HHS Reference No. E–129–2011/0–US–01).

Licensing Status: Available for licensing and commercial development.

Licensing Contacts:

• Uri Reichman, PhD, MBA; 301–435–4616; *UR7a@nih.gov.*

• John Stansberry, PhD; 301–435–5236; *js852e@nih.gov.*

Polyclonal Antibodies Against RGS7, a Regulator of G Protein Signaling, for Research and Diagnostic Use

Description of Technology: Investigators at the National Institutes of Health have generated a polyclonal antibody against the Regulator of G protein Signaling Protein 7 (RGS7). The RGS7 protein regulates neuronal G protein signaling pathways and inhibits signal transduction by increasing the GTPase activity of G protein alpha. RGS7 may play an important role in synaptic vesicle exocytosis and in the