GPR116 Knockout and Conditional Knockout Mice

Description of Technology:
Pulmonary surfactant plays a critical role in preventing alveolar collapse by decreasing surface tension at the alveolar air-liquid interface. Surfactant deficiency contributes to the pathogenesis of acute lung injury (ALI) and acute respiratory distress syndrome (ARDS), common disorders that can afflict patients of all ages and carry a mortality rate greater than 25%. Excess surfactant leads to pulmonary alveolar proteinosis. The NCI investigators created a G-protein coupled receptor GPR116 mutant mouse model and showed that GPR116 plays a previously unexpected, essential role in maintaining normal surfactant levels in the lung.

The mouse model could aid in the development of drug screens to identify agents that can modulate surfactant levels. Alveolar type II cells have also been isolated from the GPR116 wildtype and knockout mice that could be directly used in such assays. The identification of surfactant modulating agents could be important to a number of lung surfactant disorders.

Potential Commercial Applications:
Research materials to study lung surfactant homeostasis and disorders. Competitive Advantages: Not available elsewhere.

Development Stage:
- Prototype.
- Pre-clinical.
- In vitro data available.
- In vivo data available (animal).

Inventors: Bradley Dean St. Croix and Mi Young Yang (NCI).


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

Collaborative Research Opportunity:
The Center for Cancer Research Mouse Cancer Genetics Program is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize GPR116 Knockout and Conditional Knockout Mice. For collaboration opportunities, please contact John Hewes, Ph.D. at hewesj@mail.nih.gov.
Drug delivery to bones.

blood as a stem cell source.
in performing bone marrow transplants, does not exceed levels of systemic blood infusion such that intra-bone pressure and adjusts infusion pressures during sensors disposed at its proximal end directly infusing cellular therapeutics.

Characteristics (Leppla/NIAID).

Cells Having Multiple Identifying Multimeric Protein Toxins to Target Tumor Vasculature (Leppla/NIAID).

Engineered Metalloproteinase-Activated Human Cancer Therapy Using

further develop, evaluate or interested in collaborative research to capability or interest from parties.

The National Heart, Lung, and Blood Institute is seeking statements of

Collaborative Research Opportunity:

Intra-Bone Drug Delivery Device and Method

Description of Technology: The invention pertains to devices for directly infusing cellular therapeutics into patient bone. The device monitors intra-bone pressure using pressure sensors disposed at its proximal end and adjusts infusion pressures during infusion such that intra-bone pressure does not exceed levels of systemic blood pressure. Such devices, apparatus and methods are particularly suitable for use in performing bone marrow transplants, particularly transplants that utilize cord blood as a stem cell source.

Potential Commercial Applications: Drug delivery to bones.

Competitive Advantages:
• Therapeutic uptake efficiency.
• Drug delivery efficiency.
• Target specificity.

Development Stage:
• Prototype.
• In vitro data available.

Inventors: Robert Hoyt (NHLBI), Jeremy Pantin (NHLBI), Timothy Hunt (NHLBI), Randall Clevenger (NHLBI), Omer Aras (NIHCC), Richard Childs (NHLBI), Peter Choyke (NCI).


Licensing Contact: Michael Shmiovich; 301–435–5019; shmiovich@mail.nih.gov.

Collaborative Research Opportunity:
The National Heart, Lung, and Blood Institute is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize Intra-bone Drug Delivery Device and Method. For collaboration opportunities, please contact Denise Crooks at crooksd@nhlbi.nih.gov.

Method of Inducing Pluripotent or Multipotent Stem Cells by Blocking CD47 Receptor Signaling

Description of Technology: NIH researchers have discovered that blockade of the signaling activity of a single cell-surface receptor, CD47, without transfection or introduction of potentially transforming viral vectors, results in high frequency, spontaneous generation of self-renewing cells with a high proliferative capacity. Induced pluripotent stem cells (iPS cells) are currently produced by transforming cells with viral or other constitutive expression vectors encoding four stem cell transcription factors (c-Myc, Sox2, Klf4, and Oct4), but this method presents challenges such as over-expression of c-Myc, which can result in malignant transformation. The present invention relates to a method of using CD47-modulating compounds to induce multipotent stem cells without the concomitant risk of malignant transformation and without requiring the use of feeder cells. The cellular phenotypes are associated with increased expression of the hallmark stem cell-inducing transcription factors, c-Myc, Sox2, Klf4, and Oct4. The current invention builds on the NIH’s previous discoveries of antibodies, antisense morpholino oligonucleotides, peptide compounds and other small molecules that modulate CD47.

Potential Commercial Applications: Regenerative medicine and stem cell therapy.

Competitive Advantages:
• Does not require use of viral vectors.
• Eliminates risk of malignant transformation for clinical applications.
• Eliminates need for feeder cells.
• Allows generation and maintenance of a ready supply of iPS cells using a single defined agent.
• Avoids loss of differentiated phenotype associated with telomerase or T antigen transfection.

Development Stage:
• In vitro data available.
• In vivo data available (animal).

Inventors: David D. Roberts, Sukhbir Kaur, Jeff S. Isenberg (NCI).

Publications:

Intellectual Property:

• CA Application No. 2,665,287 filed 5 Oct 07.
• EP Application No. 0768382.8 filed 27 Mar 09.
• U.S. Application No. 13/546,941 filed 11 Jul 12.

Collaborative Research Opportunity:
The National Cancer Institute, Center for Cancer Research, Laboratory of Pathology, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize CD47 modulators for regenerative medicine and stem cell therapy applications. For collaboration opportunities, please contact John Hewes, Ph.D. at hewes@mail.nih.gov.

Human Monoclonal Antibodies to Glypican-3 Protein and Heparan 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. No effective treatment is available for liver cancer therapy. Glypican-3 (GPC3) is a cell surface protein that is preferentially expressed on HCC cells, making it an attractive potential target for developing a therapeutic. This invention concerns human monoclonal antibodies against GPC3 and their use for the treatment of GPC3-expressing cancers such as HCC.

Specifically, the inventors have generated two distinct human monoclonal antibodies to GPC3. The first antibody (HN3) binds to a conformational epitope on the cell surface domain of GPC3. The second antibody (HS20) binds specifically to heparan sulfate chains on GPC3. 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 toxic agent 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.

Potential Commercial Applications:
- Therapeutic antibodies against cancers that overexpress GPC3.
- Therapeutic immunotoxins or antibody-drug conjugates for killing cancer cells that overexpress GPC3.
- Diagnostics for detecting cancers associated with GPC3 overexpression.
- Specific cancers include hepatocellular cancer (HCC), melanoma, ovarian cancer, thyroid cancer, lung squamous cell carcinoma, Wilms’ tumor, neuroblastoma, hepatoblastoma, and testicular germ-cell tumors.

Competitive 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-invasive toxic alternative to current HCC treatment strategies.

Development Stage:
- Pre-clinical.
- In vitro data available.
- In vivo data available (animal).

Inventors: Mitchell Ho (NCI) et al.

Publications:


Licensing Contact: David A. Lamberton, Ph.D.; 301–435–4632; lambertsond@mail.nih.gov.

Collaborative Research Opportunity: The National Cancer Institute, 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 novel antibody or antibody-drug conjugate therapies for the treatment of liver cancer. For collaboration opportunities, please contact John Hewes, Ph.D. at hewesj@mail.nih.gov.

Dated: June 14, 2013.

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