

*Inventors:* Steven A. Rosenberg (NCI), Mark E. Dudley (NCI), Robert P. Somerville (NCI), Jianjian Jin (CC), Marianna V. Sabatino (CC), David F. Stroncek (CC).

*Intellectual Property:* HHS Reference No. E-114-2011/0—U.S. Patent Application No. 61/466,200 filed 22 March 2011.

*Related Technologies:*

- HHS Reference No. E-275-2002/1—U.S. Patent Application No. 10/526,697 filed 5 May 2005 (and foreign counterparts).

- HHS Reference No. E-273-2009/0—U.S. Patent Application No. 12/869,390 filed 26 August 2010.

*Licensing Contact:* Samuel E. Bish, PhD; 301-435-5282; bishse@mail.nih.gov.

*Collaborative Research Opportunity:* The National Cancer Institute Surgery Branch is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize gas permeable flasks for cell and gene therapy applications and multicenter clinical trials. For collaboration opportunities, please contact John Hewes, PhD, at hewesj@mail.nih.gov.

**A Novel Optomechanical Module that Enables a Conventional Inverted Microscope To Provide Selective Plane Illumination Microscopy (iSPIM)**

*Description of Technology:* The invention describes an optomechanical module that, when engaged with a conventional inverted microscope, provides selective plane illumination microscopy (iSPIM). The module is coupled to the translational base of the microscope whereby a SPIM excitation objective is engaged to one portion of the mount body, and a SPIM detection objective (having a longitudinal axis perpendicular to that of the excitation objective) is engaged to another portion of the mount body. Such a system offers the advantages of SPIM (optically sectioned, high-speed volumetric interrogation of living samples, enabling, for example, the study of developmental or neuronal dynamics at high frame rates), while maintaining the flexibility and sample geometry of commercially available inverted microscopes (thus additionally allowing wide-field, TIRF, confocal, or 2 photon imaging of samples).

*Potential Commercial Applications:* The microscope can be used for:

- Imaging of live whole animals (e.g. worms) (demonstrated already).
- Superresolution (photoactivated localization microscopy) with minimal bleaching of dye molecules.

- High speed investigation of neuronal dynamics at high frame rates.

*Competitive Advantages:*

- The system offers the advantages of SPIM, while maintaining the flexibility and sample geometry of commercially available inverted microscopes.

- In this system the sample can be easily mounted on a rectangular coverslip and may be translated using an automated 3D mechanical stage and additionally imaged using the conventional light path built into the inverted microscope frame.

*Development Stage:*

- Prototype.
- In vivo data available (animal).

*Inventors:* Hari Shroff (NIBIB) *et al.*

*Publication:* A publication is under review at PNAS.

*Intellectual Property:* HHS Reference No. E-078-2011/0—U.S. Provisional Patent Application No. 61/449,422 filed 04 Mar 2011.

*Licensing Contact:* Michael Shmilovich, Esq.; 301-435-5019; shmilovm@mail.nih.gov.

*Collaborative Research Opportunity:* The NIBIB is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize applications of the invention. For collaboration opportunities, please contact Hari Shroff at 301-435-1995 or hari.shroff@nih.gov.

**A Vaccine for *Shigella sonnei* for Both Children and Adults**

*Description of Technology:* There is currently no vaccine widely available for shigellosis, which affects over 150 million people worldwide and causes over 1 million deaths a year, mostly children. The present invention discloses a novel immunogen to be used in a vaccine for both children and adults. The immunogen, a low-molecular mass O-SP-core fragment, generates high antibody responses in animal studies, which means reduced number of vaccinations. The immunogen is easy to isolate for ease of manufacturing. Additionally, the methods of manufacturing vaccines and protocols of preventing and/or treating Shigellosis had been carried out in the present invention.

*Potential Commercial Applications:* *Shigella sonnei* vaccines and diagnostics.

*Competitive Advantages:*

- Vaccine can be used in both children and adults.
- Doses of vaccine are reduced.
- Immunogen is easy to isolate for easy vaccine production.

*Development Stage:*

- Prototype.

- Pilot.
- Early-stage.
- Pre-clinical.
- In vitro data available.
- In vivo data available (animal).

*Inventors:* John B. Robbins, Rachel Schneerson, Joanna Kubler-Kielb, Christopher P. Mocca (NICHD).

*Publications:*

1. Robbins JB, *et al.* Synthesis, characterization, and immunogenicity in mice of *Shigella sonnei* O-specific oligosaccharide-core-protein conjugates. *Proc Natl Acad Sci U S A.* 2009 May 12;106(19):7974-7978. [PMID 19346477]

2. Kubler-Kielb J, *et al.* The elucidation of the structure of the core part of the LPS from *Plesiomonas shigelloides* serotype O17 expressing O-polysaccharide chain identical to the *Shigella sonnei* O-chain. *Carbohydr Res.* 2008 Dec 8;343(18):3123-3127. [PMID 18954864].

*Intellectual Property:* HHS Reference No. E-308-2008/0—

- PCT Application No. PCT/US2009/053897 filed 14 Aug 2009.

- U.S. Application No. 13/059,051 filed 14 Feb 2011.

*Licensing Contact:* Susan Ano, PhD; 301-435-5515; anos@mail.nih.gov.

Dated: August 29, 2011.

**Richard U. Rodriguez,**

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

[FR Doc. 2011-22693 Filed 9-2-11; 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.

**Antibodies Against TL1A, a TNF-Family Cytokine, for the Treatment and Diagnosis of Autoimmune Inflammatory Diseases**

*Description of Technology:* Autoimmune inflammatory diseases occur in greater than five percent of the United States population; this disease group includes asthma, multiple sclerosis, rheumatoid arthritis, and lupus. Treatments generally include immunosuppressants or anti-inflammatory drugs, which can have serious side effects; recently, more specific immunomodulatory therapies such as TNF-alpha antagonists have been developed.

In experiments with mice, NIAMS inventors have shown that the interaction between the TNF family ligand TL1A with its receptor, DR3, is critical for development of disease in asthma, inflammatory bowel disease and multiple sclerosis. They have also developed anti-TL1A antibodies that prevent disease in mouse models of rheumatoid arthritis and inflammatory bowel disease.

This technology describes anti-mouse TL1A and anti-human TL1A monoclonal antibodies that may be useful for the development of diagnostics and therapeutics for autoimmune inflammatory disease, as well as methods of treating such disease by blocking the interaction between TL1A and DR3.

*Potential Commercial Applications:*

- Antibody-based therapeutics for autoimmune inflammatory disease.
- Diagnostics for autoimmune inflammatory disease.
- Research tools to probe the role of TL1A-DR3 interactions in the development of autoimmune disease.

*Competitive Advantages:*

- Specific immunomodulatory effect provides potential for potent therapy without inducing global immunosuppression.
- Anti-TL1A monoclonal antibodies available for further development.

*Development Stage:*

- Early-stage.
- In vitro data available.
- In vivo data available (animal).

*Inventors:* Richard M. Siegel, Francoise Meylan, Yun-Jeong Song (NIAMS).

*Publication:* Meylan F, *et al.* The TNF-family cytokine TL1A drives IL-

13-dependent small intestinal inflammation. *Mucosal Immunol.* 2011 Mar;4(2):172-185. [PMID 20980995].

*Intellectual Property:*

- HHS Reference No. E-011-2007/0—U.S. Application No. 11/972,395 filed 10 Jan 2008.
- HHS Reference No. E-073-2011/0—U.S. Application No. 61/488,671 filed 20 May 2011.

*Related Technology:* HHS Reference No. E-072-2011/0—Research Tool. Patent protection is not being pursued for this technology.

*Licensing Contact:* Tara L. Kirby, PhD; 301-435-4426; [tarak@mail.nih.gov](mailto:tarak@mail.nih.gov).

*Collaborative Research Opportunity:* The National Institute of Arthritis and Musculoskeletal and Skin Diseases is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize the anti-mouse TL1A and anti-human TL1A monoclonal antibodies. For collaboration opportunities, please contact Cecilia Pazman at [pazmance@mail.nih.gov](mailto:pazmance@mail.nih.gov).

**TL1A Transgenic Mice for the Study of Inflammatory Bowel Disease (IBD) and Allergic-Type Immune Responses**

*Description of Technology:* TL1A is a TNF family cytokine that co-stimulates T-cell proliferation and cytokine production through its interactions with the TNF family receptor DR3. TL1A-DR3 interactions have been shown to be important for the development of autoimmune inflammatory diseases, including inflammatory bowel disease (IBD).

In order to probe the role of TL1A-DR3 interactions in IBD, NIAMS inventors have developed transgenic mice that constitutively express TL1A in T cells or in dendritic cells. These mice spontaneously develop inflammatory small bowel pathology that is IL-13 dependent, and that closely resembles intestinal responses to allergens and to nematode infection.

These mice represent a unique model for the study of IBD, and in particular, the role of IL-13 in the development of this disease. They may also be used as a platform for investigating agents that block TL1A-DR3 interactions and the pathology associated with chronic TL1A expression.

*Potential Commercial Applications:*

- Studies of small bowel inflammation/IBD.
- Studies of the role of TL1A-DR3 interactions in the development of autoimmune inflammatory disease.
- Investigation of TL1A-DR3 blocking agents for the treatment of IBD or other TL1A-DR3 dependent diseases.

*Competitive Advantages:*

- Lines available with transgene expressed in T cells (under CD2 promoter) or dendritic cells (CD11c promoter).
- Models are IL-13 dependent.
- No major defects in systemic immunity.

*Development Stage:* In vivo data available (animal).

*Inventors:* Richard M. Siegel and Francoise Meylan (NIAMS).

*Publications:*

1. Meylan F, *et al.* The TNF-family cytokine TL1A drives IL-13-dependent small intestinal inflammation. *Mucosal Immunol.* 2011 Mar;4(2):172-185. [PMID 20980995].

2. Meylan F, *et al.* The TNF-family receptor DR3 is essential for diverse T cell-mediated inflammatory diseases. *Immunity.* 2008 Jul 18;29(1):79-89. [PMID 18571443].

*Intellectual Property:* HHS Reference No. E-072-2011/0—Research Tool. Patent protection is not being pursued for this technology.

*Related Technologies:*

- HHS Reference No. E-011-2007/0—U.S. Application No. 11/972,395 filed 10 Jan 2008.
- HHS Reference No. E-073-2011/0—U.S. Application No. 61/488,671 filed 20 May 2011.

*Licensing Contact:* Tara L. Kirby, PhD; 301-435-4426; [tarak@mail.nih.gov](mailto:tarak@mail.nih.gov).

*Collaborative Research Opportunity:* The National Institute of Arthritis and Musculoskeletal and Skin Diseases is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize TL1A Transgenic Mice. For collaboration opportunities, please contact Cecilia Pazman at [pazmance@mail.nih.gov](mailto:pazmance@mail.nih.gov).

**Human Monoclonal Antibodies Cross-reacting to Insulin-like Growth Factors IGF-I and IGF-II as Potential Anti-tumor Agents**

*Description of Technology:* The type 1 insulin-like growth factor (IGF) receptor (IGF1R) is over-expressed by many tumors and mediates proliferation, motility, and protection from apoptosis. Agents that inhibit IGF1R expression or function can potentially block tumor growth and metastasis. Its major ligands, IGF-I, and IGF-II are over-expressed by multiple tumor types. Previous studies indicate that inhibition of IGF-I, and/or IGF-II binding to its cognizant receptor negatively modulates signal transduction through the IGF pathway and concomitant cell proliferation and growth. Therefore, use of humanized or fully human antibodies against IGFs

represents a valid approach to inhibit tumor growth.

The present invention discloses the identification and characterization of a fully human monoclonal antibody designated m708.5 that has been affinity matured against IGF-I and IGF-II and displays extremely high affinities for IGF-I and IGF-II in the pM range. The m708.5 antibody potently inhibited signal transduction mediated by the IGF-1R interaction with IGF-I and IGF-II and blocked phosphorylation of IGF-1R and the insulin receptor. Further, this antibody inhibited migration in the MCF-7 breast cancer cell line at the pM range. Therefore, this antibody can be used to prevent binding of IGF-I and/or IGF-II to its concomitant receptor IGF1R, consequently, modulating diseases such as cancer.

**Potential Commercial Applications:**

- Therapeutic for the treatment of various human diseases associated with aberrant cell growth and motility such as breast, prostate, and leukemia carcinomas.
- Research reagent to study IGF-I and/or IGF-II binding and its association with tumor growth.

**Competitive Advantages:**

- Antibodies against the ligands IGF-I and IGF-II, such as this invention, inhibit the interaction with IGF-1R yet likely do not have the type of toxicity associated with IGF-1R antibodies.
- High concentrations of IGF-II are found in cancer patients, on average several fold higher than IGF-I, thus this cross-reacting IGF-I/IGF-II antibody could be more effective than existing IGF-1R and/or IGF-I currently in the clinic.

- This novel IGF antibody may provide therapeutic intervention for multiple carcinomas.

**Development Stage:**

- Pre-clinical.
- In vitro data available.

**Inventors:** Dimiter Dimitrov, Zhongyu Zhu, and Qi Zhao (NCI).

**Publications:**

1. Zhao Q, *et al.* Human monoclonal antibody fragments binding to insulin-like growth factors 1 and 2 with picomolar affinity. *Mol Cancer Ther.* 2011 Jul 12; Epub ahead of print. [PMID 21750218].

2. Feng Y, *et al.* Novel human monoclonal antibodies to insulin-like growth factor (IGF)-II that potently inhibit the IGF receptor type I signal transduction function. *Mol Cancer Ther.* 2006;5(1):114-120. [PMID 18283605].

3. Kimura T, *et al.* Targeting of bone-derived insulin-like growth factor-II by a human neutralizing antibody suppresses the growth of prostate cancer

cells in a human bone environment. *Clin Cancer Res.* 2010 Jan 1;16(1): 121-129. [PMID 20028742].

**Intellectual Property:** HHS Reference No. E-068-2011/0—U.S. Provisional Application No. 61/474,664 filed 12 April 2011.

**Related Technologies:**

- HHS Reference No. E-336-2005/0—U.S. Patent Application No. 12/296,328 filed 07 Oct 2008; Antibody Compositions and Methods for Treatment of Neoplastic Disease.
- HHS Reference No. E-217-2005/0—U.S. Patent No. 7,824,681 issued 02 Nov 2010; Human Monoclonal Antibodies that Specifically Bind IGF-II.

**Licensing Contact:** Whitney Hastings; 301-451-7337; [hastingw@mail.nih.gov](mailto:hastingw@mail.nih.gov).

**Collaborative Research Opportunity:** The NCI CCR Nanobiology Program, Protein Interaction Group, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology. For collaboration opportunities, please contact John Hewes, PhD at [hewesj@mail.nih.gov](mailto:hewesj@mail.nih.gov).

**Transgenic Mice Expressing Human Arginase II Gene in Endothelium: Useful for Studying Atherosclerosis and Other Vasculopathies**

**Description of Technology:**

Cardiovascular disorders associated with endothelial dysfunction, like atherosclerosis, have decreased endothelial nitric oxide (NO) bioavailability. L-arginine, the primary substrate for endothelial nitric oxide synthase (eNOS), is important in the regulation of NO production. Arginase competes with eNOS for L-arginine and has been implicated in the endothelial dysfunction. NIH investigators have generated transgenic mice with human ArgII (hArgII) gene under control of endothelial-specific Tie2 promoter. In these mice, hArgII was expressed at very high levels in all tissues except liver. Analysis has shown that expression of hArgII was endothelium-specific. Overexpression of hArgII neither led to significant changes in plasma level of arginine, citrulline, NOHA, ADMA, SDMA and ornithine, nor to changes in plasma lipid levels. Level of arginase activity in peritoneal macrophages isolated from the transgenic mice also was also unchanged. However, ArgII overexpression induced signs of endothelial dysfunction. In apoE-knockout mice hArgII led to 2-fold increasing in aortic area with atherosclerotic lesions. The Tie2hArgII transgenic mouse can be useful as a new model for investigating the role of ArgII

in endothelial function and development of atherosclerosis.

**Potential Commercial Applications:**

- Useful to study the role of arginase II gene in endothelium.
- Useful for testing the drugs for treatment of the endothelial dysfunction related to eNOS insufficiency, including hypertension.
- Useful to study mechanisms of atherosclerosis.

**Competitive Advantages:** Better model system to study functional significance of arginase II.

**Development Stage:**

- Early-stage.
- Pre-clinical.
- In vivo data available (animal).

**Inventors:** Boris L. Vaisman and Alan T. Remaley (NHLBI).

**Publication:** Vaisman BL, *et al.* Abstract 3636: The Effects of Arginase II Overexpression on Endothelial Function in Transgenic Mouse Model. *Circulation.* 2008 Oct 28;118:S 455.

**Intellectual Property:** HHS Reference No. E-255-2010/0—Research Tool. Patent protection is not being pursued for this technology.

**Licensing Contact:** Suryanarayana (Sury) Vepa, PhD; 301-435-5020; [vepas@mail.nih.gov](mailto:vepas@mail.nih.gov).

Dated: August 29, 2011.

**Richard U. Rodriguez,**

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

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**BILLING CODE 4140-01-P**

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**National Institutes of Health**

**National Center for Complementary & Alternative Medicine; Notice of Closed Meeting**

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. App.), notice is hereby given of the National Advisory Council for Complementary and Alternative Medicine (NACCAM) meeting.

The meeting will be open to the public as indicated below, with attendance limited to space available. Individuals who plan to attend and need special assistance, such as sign language interpretation or other reasonable accommodations, should notify the Contact Person listed below in advance of the meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections