Modification of Recombinant Anti-Tumor RNase (rapLR1) for Optimal Use in the Large Scale Manufacture of Stable and Potent RapLR1-Antibody Conjugates

Description of Technology: This technology involves modified rapLR1 molecules having an improved capacity for conjugation to targeting moieties. Previously, techniques for attaching wild-type rapLR1 to a targeting moiety required an excess of RNase, leading to high production costs. The inventors have now mutated specific amino acids in rapLR1 to allow a more efficient (and therefore less costly) conjugation reaction.

Members of the ribonuclease A (RNase A) superfamily, such as rapLR1, have the ability to efficiently kill a wide range of cancer cells. Ligand binding moieties such as antibodies or peptides can be used to target RNases to a particular cell or cell type that expresses a marker, e.g., a marker that is associated with cancer. The current invention provides rapLR1 molecules that have been genetically modified to contain a cysteine at a specific location that does not interfere with the enzymatic activity of the molecule. The inserted cysteine provides the advantage of a site-directed and specific attachment of rapLR1 to targeting moieties, which results in more efficient production of the therapeutic. This significantly reduces the cost of bringing rapLR1-related cancer therapeutics to market.

Applications: Targeted anti-cancer therapy molecules; Targeting moiety can be interchanged based on target cancer cells; Targeting any disease in which the cell is transformed and presents unique levels of cell surface markers.

Advantages: RapLR1 delivery, specificity and toxicity to cancer cells is increased by conjugation to a targeting moiety; Modified rapLR1 increases conjugation efficiency, making the preparation of the anti-cancer agents more cost effective without sacrificing specificity.

Benefits: Cancer is the second leading cause of death in the United States, with approximately 600,000 cancer-related deaths occurring in 2006 alone. Because rapLR1 can be used to treat a number of different cancers (depending on the targeting moiety), there is a powerful social benefit from this technology: Improving the duration and quality of life of a wide range of cancer patients. Furthermore, the cancer therapeutic market is expected to reach $27 billion by 2009. Because rapLR1 can now be efficiently conjugated to targeting moieties, there is an opportunity to occupy a significant niche in that predicted market, with lower cost to the licensee.

Inventors: Dianne L. Newton et al. (NCI).

U.S. Patent Status: Pending PCT Application PCT/US2006/038180, published as WO 2007/041361 (HHS Reference No. E–265–2005/0–PCT–02).

Licensing Contact: David A. Lambertson, PhD; Phone: (301) 435–4632; Fax: (301) 402–0220; E-mail: *lambertsond@mail.nih.gov.*

Methods for Expression and Purification of Immunotoxins

Description of Technology: The invention concerns immunotoxins and methods of making the immunotoxins. Targeting of the immunotoxins occurs via an antibody that is specific to T cells. This allows the specific ablation of malignant T cells and resting T cells. The transient ablation of resting T cells can ''reset'' the immune system by accentuating tolerizing responses. As a result, the immunotoxin can be used to treat autoimmune disease, malignant T cell-related cancers, and graft-versus-host disease. The toxin portion of the immunotoxin is engineered to maintain bioactivity when produced in yeast, specifically *Pichia pastoris.* This system allows the production of dimeric antibody fragments with increased binding affinity and potency.

Applications: Immunotoxins produced by this method can be used for the treatment of autoimmune diseases such as multiple sclerosis, lupus, type I diabetes, aplastic anemia; Immunotoxins produced by this method can be used for treatment of T-cell leukemias and lymphomas such as cutaneous T cell leukemia/lymphoma (CTCL); Immunotoxins produced by this method can be used for increasing immune tolerance in patients requiring transplants/grafts.

Advantages: Method produces GMP quality immunotoxin and can be scaled up to industry scales; Modified toxin moiety has reduced glycosylation in this system, resulting in a more effective and efficient immunotoxin; Immunotoxin doesn't produce the deleterious side-effects seen with other methods of treating autoimmune disease, malignant T cell leukemia/lymphoma and graft-versus-host disease.

Benefits: New methods and compositions with limited side-effects have the potential to revolutionize treatment of autoimmune disease; provides an opportunity to capture a significant market share for the millions of people who suffer from an autoimmune disease.

Inventors: *David Neville* et al. (NIMH)

Patent Status: U.S. Patent Application No. 10/566,886 filed 01 Feb 2006, which published as U.S. 2006/0216782 on 28 Sep 2006 (HHS Reference No. E–043–1997/2–US–03); U.S. Patent No. 6,632,928 issued 14 Oct 2003 (HHS Reference No. E–044–1997/0–US–07); U.S. Patent Application No. 10/435,567 filed 09 May 2003, which published as 2003/0185825 on 02 Oct 2003 (HHS Reference No. E–044–1997/0–US–08); U.S. Patent Application No. 10/296,085 filed 18 Nov 2002, which published as 2004/0127682 on 01 Jul 2004 (HHS Reference No. E–044–1997/1–US–06); Foreign rights are also available.

Licensing Status: Available for exclusive or non-exclusive licensing.

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

Collaborative Research Opportunity: The National Institute of Mental Health, Laboratory of Molecular Biology, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize methods of expression and purification of immunotoxins. Please contact David Neville at *davidn@mail.nih.gov* for more information.

Dated: June 28, 2007.

Steven M. Ferguson,

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

[FR Doc. E7–13128 Filed 7–5–07; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institutes of Neurological Disorders and Stroke; Notice of Closed Meetings

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. appendix 2), notice is hereby given of the following meetings.

The meetings will be closed to the public in accordance with the provisions set forth in section 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material , and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Institutes of Neurological Disorders and Stroke Special Emphasis Panel, Texas–SNRP.

Date: July 16–17, 2007.

Time: 8 a.m. to 1 p.m.

Agenda: To review and evaluate grant applications.

Place: Marriott San Antonio Riverwalk, 711 East River Walk, San Antonio, TX 78205.

Contact Person: Philip F. Wiethorn, Scientific Review Administrator, DHHS/NIH/NINDS/DER/SRB, 6001 Executive Boulevard; MSC 9529, Neuroscience Center; Room 3203, Bethesda, MD 20892–9529, (301) 496–5388, *wiethorp@ninds.nih.gov.*

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

Name of Committee: National Institutes of Neurological Disorders and Stroke Special Emphasis Panel, Neurofibromatosis/Tuberous Sclerosis.

Date: July 24, 2007.

Time: 11 a.m. to 5 p.m.

Agenda: To review and evaluate grant applications.

Place: National Institutes of Health, Neuroscience Center, 6001 Executive Boulevard, Rockville, MD 20852 (Telephone Conference Call).

Contact Person: Shantadurga Rajaram, PHD, Scientific Review Administrator, Scientific Review Branch, NIH/NINDS/Neuroscience Center, 6001 Executive Blvd., Suite 3208, Msc 9529, Bethesda, MD 20852, (301) 435–6033, *rajarams@mail.nih.gov.*

The notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

(Catalogue of Federal Domestic Assistance Program Nos. 93.853, Clinical Research Related to Neurological Disorders; 93.854, Biological Basis Research in the Neurocsciences, National Institutes of Health, HHS)

Dated: June 29, 2007.

Anna Snouffer,

Acting Director, Office of Federal Advisory Committee Policy.

[FR Doc. 07–3292 Filed 7–5–07; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Child Health and Human Development; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The contract proposals and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the contract proposals, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Institute of Child Health and Human Development Special Emphasis Panel, International and Domestic Pediatric and Maternal HIV Studies Coordinating Center.

Date: July 31, 2007.

Time: 11:55 a.m. to 1:30 p.m.

Agenda: To review and evaluate contract proposals.

Place: National Institutes of Health, 6100 Executive Boulevard, Rockville, MD 20852 (Telephone Conference Call).

Contact Person: Hameed Khan, PhD, Scientific Review Administrator, Division of Scientific Review, National Institute of Child Health and Human Development, NIH, 6100 Executive Blvd., Room 5B01 Bethesda, MD 20892, (301) 435–6902, *khanh@mail.nih.gov.*

(Catalogue of Federal Domestic Assistance Program Nos. 93.864, Population Research; 93.865, Research for Mothers and Children; 93.929, Center for Medical Rehabilitation Research; 93.209, Contraception and Infertility Loan Repayment Program, National Institutes of Health, HHS)

Dated: June 29, 2007.

Anna Snouffer,

Acting Director, Office of Federal Advisory Committee Policy.

[FR Doc. 07–3294 Filed 7–5–07; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute on Drug Abuse; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Institute on Drug Abuse Special Emphasis Panel, Imaging of Drug Use Prevention Messages (R21).

Date: July 24, 2007.

Time: 8 a.m. to 6 p.m.

Agenda: To review and evaluate grant applications.

Place: The Fairmont Washington, DC, 2401 M Street, NW, Washington, DC 20037.

Contact Person: Mark R. Green, PhD, Deputy Director, Office of Extramural Affairs, National Institute on Drug Abuse, NIH, DHHS, Room 220, MSC 8401, 6101 Executive Boulevard, Bethesda, Md 20892–8401, (301) 435–1431, *mgreen1@nida.nih.gov.*

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

(Catalogue of Federal Domestic Assistance Program Nos. 93.279, Drug Abuse and Addiction Research Programs. National Institutes of Health, HHS)

Dated: June 29, 2007.

Anna Snoufer,

Acting Director, Office of Federal Advisory Committee Policy.

[FR Doc. 07–3295 Filed 7–05–07; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute on Aging; Notice of Closed Meetings

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meetings.

The meetings will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Institute on Aging Special Emphasis Panel, Cognition and Hippocampal Aging.

Date: July 17, 2007.

Time: 1 p.m. to 4 p.m.

Agenda: To review and evaluate grant applications.

Place: National Institute on Aging, Gateway Building, 7201 Wisconsin Avenue, 2C212, Bethesda, MD 20814 (Telephone Conference Call).

Contact Person: William Cruce, PhD, Health Scientist Administrator, Scientific Review Office, National Institute on Aging, National Institutes of Health, Room 2C212, 7201 Wisconsin Avenue, Bethesda, MD 20814, 301–402–7704, *crucew@nia.nih.gov.*