

from a patient (R2) with broadly HIV-1 neutralizing antibodies. *Virology*. 2007 Jun 20;363(1):79–90.

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7. Z Zhu, KN Bossart, KA Bishop, G Cramer, AS Dimitrov, JA McEachern, Y Feng, D Middleton, LF Wang, CC Broder, DS Dimitrov. Exceptionally potent cross-reactive neutralization of Nipah and Hendra viruses by a human monoclonal antibody. *J Infect Dis*. 2008 Mar 15;197(6):846–853.

8. MY Zhang, BK Vu, A Choudhary, H Lu, M Humbert, H Ong, M Alam, RM Ruprecht, G Quinnan, S Jiang, DC Montefiori, JR Mascola, CC Broder, BF Haynes, DS Dimitrov. Cross-reactive human immunodeficiency virus type 1-neutralizing human monoclonal antibody which recognizes a novel conformational epitope on gp41 and lacks reactivity against self antigens. *J Virol*. 2008 Jul;82(14):6869–6879.

**Patent Status:** U.S. Provisional Application No. 61/104,706 filed 11 Oct 2008 (HHS Reference No. E-322–2008/0–US–01).

**Licensing Status:** Available for licensing.

**Licensing Contact:** Sally Hu, Ph.D.; 301–435–5606; [HuS@mail.nih.gov](mailto:HuS@mail.nih.gov).

**Collaborative Research Opportunity:** The National Cancer Institute is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this method. Please contact John D. Hewes, Ph.D. at 301–435–3121 or [hewesj@mail.nih.gov](mailto:hewesj@mail.nih.gov) for more information.

#### Anti-Hepatitis C Virus Activity of the Protein Scytovirin (SVN)

**Description of Technology:** The invention provides compositions and methods of use for potent anti-HCV protein scytovirin to prevent and treat HCV infections. Currently there is neither effective treatment nor vaccine against HCV infection and chronic HCV infection may lead to liver cancer and death. Scytovirin can be used alone or in combination with other anti-HCV drugs for HCV treatment and prevention.

**Applications:** The treatment and prevention of HCV infections.

**Advantages:** Potent anti-HCV activity; Can be applied both systematically or locally.

**Development Status:** *In vitro* data available.

**Market:** HCV therapeutics and preventatives.

**Inventors:** Barry R. O'Keefe et al. (NCI).

**Publications:** Data collection and manuscripts may be submitted in 2009.

**Patent Status:** U.S. Provisional Application No. 61/137,511 filed 31 Jul 2008 (HHS Reference No. E-161–2008/0–US–01).

**Related Technology:** HHS Reference No. E-017–2002/0—Scytovirins and Related Conjugates, Antibodies, Compositions, Nucleic Acids, Vectors, Host Cells, Methods of Production and Methods of Using Scytovirin.

**Licensing Status:** Available for licensing.

**Licensing Contact:** Sally Hu, Ph.D.; 301–435–5606, [HuS@mail.nih.gov](mailto:HuS@mail.nih.gov).

**Collaborative Research Opportunity:** The National Cancer Institute CCR Molecular Targets Development Program is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology. Please contact John D. Hewes, Ph.D. at 301–435–3121 or [hewesj@mail.nih.gov](mailto:hewesj@mail.nih.gov) for more information.

Dated: March 19, 2009.

**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

#### 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.

#### Treatment of Schistosomiasis Using Substituted Oxadiazole 2-Oxides

**Description of Technology:** Available for licensing and commercial development are pharmaceutical compositions and methods for the treatment of schistosomiasis in mammals. The various compositions are based on a number of compounds derived from 1,2,5-oxadiazole that are potent inhibitors of thioredoxin glutathione reductase (TGR), a critical parasite redox protein.

Schistosomiasis is a chronic disease caused by trematode flatworms of the genus *Schistosoma*, including *S. mansoni*, *S. japonicum* and *S. haematobium*. Adult schistosome parasites live in an aerobic environment within human hosts, and therefore must have effective mechanisms to maintain cellular redox balance. Additionally, the worms must be able to evade reactive oxygen species generated by the host's immune response. In most eukaryotes there are two major systems to detoxify reactive oxygen species, one based on the tripeptide glutathione and the other based on the protein thioredoxin. Glutathione reductase (GR) reduces glutathione disulfide, whereas thioredoxin reductases (TrxR) are pivotal in the Trx-dependent system. It was recently discovered that specialized TrxR and GR enzymes are absent in schistosomes. Instead, they are replaced by the unique multifunctional enzyme TGR. This reliance on a single enzyme for both glutathione disulfide and thioredoxin reduction suggests that the parasite's redox systems are subject to a bottleneck dependence on TGR, and that TGR represents a potentially important drug target.

Schistosomiasis remains a major and neglected health problem in many tropical areas. The health burden resulting from schistosomiasis is estimated to include more than 200 million people infected, 779 million at risk of infection, 280,000 deaths annually, and more than 20 million individuals experiencing high morbidity. Clinical manifestations of schistosomiasis infection include abdominal pain, cough, diarrhea,

eosinophilia, fever, fatigue, and hepatosplenomegaly. The primary route of infection occurs through contact with infected river and lake water, at which time the parasite burrows into the skin, matures, then migrates to other areas of the body. Adult schistosome parasites reside in the mesenteric veins of their human hosts, where they can survive for up to 30 years. The need to control schistosomiasis is acute and efforts have been ongoing for years on three main fronts: Prevention (via establishment and maintenance of sources of safe potable water), development of a vaccine, and use of drugs to treat the infection.

**Applications:** Treatment of schistosomiasis.

**Advantages:** The specific inhibition of TGR by the composition of this invention could satisfy the current need for new broad spectrum drugs to treat schistosomiasis, given the limitations of other drugs currently used or under development. Praziquantel, the only drug currently used against the infection, although stable, effective and relatively inexpensive, must be administered on an annual or semi-annual basis. Furthermore, there are preliminary reports of praziquantel-resistant cases. Artemisinin has shown promise as a new drug for the treatment of schistosomiasis, but its use must be restricted in areas of malaria transmission so that its use as an antimalarial is not put at risk. Oxamniquine, a tetrahydroquinoline derivative, is effective only against *S. mansoni* and resistance has been reported, further reducing its potential value in schistosomiasis control.

**Development Status:** To date, the general oxadiazole-2-oxide chemotype described here has shown efficacy in animal models. Efforts to define the pharmacophore and optimize this chemotype in terms of potency, efficacy and selectivity will be reported in due course. Currently, selected oxadiazole-2-oxides are being evaluated in advanced ADME/T assays and are being formulated for oral dosing experiments.

**Inventors:** Craig J. Thomas (NHGRI) *et al.*

#### **Publications**

1. G Rai *et al.* Structure-mechanism insights and the role of nitric oxide donation guide the development of oxadiazole-2-oxides as targeted agents against Schistosomiasis. In preparation.

2. G Rai, CJ Thomas, W Leister, DJ Maloney. Synthesis of oxadiazole-2-oxide analogues as potential antischistosomal agents. Tetrahedron Lett., accepted.

3. AA Sayed, A Simeonov, CJ Thomas, J Inglese, CP Austin, DL Williams. Identification of oxadiazoles as new drug leads for the control of schistosomiasis. Nat Med. 2008 Apr;14(4):407–412.

4. A Simeonov, A Jadhav, AA Sayed, Y Wang, ME Nelson, CJ Thomas, J Inglese, DL Williams, CP Austin. Schistosoma mansoni thioredoxin-glutathione reductase (TGR) inhibitors identified via quantitative high-throughput screen. PLoS Negl Trop Dis. 2007;2:1–10.

**Patent Status:** U.S. Provisional Application No. 61/088,970 filed 14 Aug 2008, entitled "Oxadiazole-2-Oxides as Antischistosomal Agents" (HHS Reference No. E-162-2008/0-US-01).

**Licensing Status:** Available for licensing.

**Licensing Contact:** Cristina Thalhammer-Reyero, Ph.D., MBA; 301-435-4507; [thalhamc@mail.nih.gov](mailto:thalhamc@mail.nih.gov).

**Collaborative Research Opportunity:** The NIH Chemical Genomics Center is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize appropriate lead compounds described in U.S. Provisional Application No. 61/088,970. Please contact Dr. Craig J. Thomas via e-mail ([craig@nhgri.nih.gov](mailto:craig@nhgri.nih.gov)) for more information.

#### **Dendrimer Conjugates Targeting Adenosine Receptors, P2Y Receptors and Other Receptors of the GPCR Superfamily, for Use in the Treatment of Various Disorders, Including Neurodegenerative Diseases, Stroke, Epilepsy, Pain and Thrombosis**

**Description of Technology:** Available for licensing and commercial development are conjugate compositions useful in the treatment of a variety of diseases, comprising a dendrimer and a ligand. The ligand is a functionalized congener of an agonist or antagonist of a receptor of the G-protein coupled receptor (GPCR) superfamily. More specifically, the invention focuses on several agonists and antagonists of A<sub>1</sub>, A<sub>2A</sub>, A<sub>2B</sub>, and A<sub>3</sub> adenosine receptors and P2Y receptors, all members of the GPCR superfamily. For example, an agonist of the A<sub>1</sub> adenosine receptor is useful for treating a number of diseases including neurodegeneration, stroke, epilepsy, and pain. Antithrombotic treatment is another example of the use of this dendrimer technology. Dendrimers are polymers made from branched monomers through the iterative organic synthesis by adding one layer at each

step to provide a symmetrical structure. Certain drugs, such as taxol, cisplatin, methotrexate, and ibuprofen, have been covalently linked to dendrimers in a reversible fashion. However, dendrimer conjugates in this application are biologically active without cleavage of the drug or cellular uptake. The conjugate of the invention can include any suitable dendrimer, particularly a poly(amidoamine) (PAMAM) dendrimer. The invention further provides pharmaceutical compositions and methods of treating various diseases and diagnostic methods employing such conjugates.

#### **Applications**

- Treatment of a number of diseases involving receptors of the GPCR superfamily.
- Determination of a potential treatment of a patient with an agonist or antagonist or receptors of the GPCR superfamily.

**Advantages:** The dendrimer conjugates described in this invention have one or more advantages over corresponding monomeric drugs, including altered pharmacokinetics, decreased toxicity, increased solubility, enhanced potency or selectivity due to the multivalency.

**Development Status:** The development is still in the early stages.

**Inventors:** Kenneth A. Jacobson *et al.* (NIDDK).

**Relevant Publications:** The published patent applications are listed below. In addition, the technology is further described in the following publications:

1. Y Kim, B Hechler, A Klutz, C Gachet, KA Jacobson. Toward multivalent signaling across G protein-coupled receptors from poly(amidoamine) dendrimers. Bioconjug Chem. 2008 Feb;19(2):406–411.

2. Y Kim, AM Klutz, KA Jacobson. Systematic investigation of polyamidoamine dendrimers surface-modified with poly(ethylene glycol) for drug delivery applications: Synthesis, characterization, and evaluation of cytotoxicity. Bioconjug Chem. 2008 Aug;19(8):1660–1672.

3. Y Kim, AM Klutz, B Hechler, ZG Gao, C Gachet, KA Jacobson. Application of the functionalized congener approach to dendrimer-based signaling agents acting through A<sub>2A</sub> adenosine receptors. Purinergic Signal. 2009 Mar;5(1):39–50.

4. AA Ivanov and KA Jacobson. Molecular modeling of a PAMAM-CGS21680 dendrimer bound to an A<sub>2A</sub> adenosine receptor homodimer. Bioorg Med Chem Lett. 2008 Aug 1;18(15):4312–4315.

5. AM Klutz, ZG Gao, J Lloyd, A Shainberg, KA Jacobson. Enhanced A<sub>3</sub> adenosine receptor selectivity of multivalent nucleoside-dendrimer conjugates. *J Nanobiotechnol.* 2008 Oct 23;6:12.

#### Patent Status

- U.S. Provisional Application No. 60/947,121 filed 20 Jun 2007 (HHS Reference No. E-219-2007/0-US-01).
- U.S. Provisional Application No. 61/045,498 filed 16 Apr 2008 (HHS Reference No. E-219-2007/1-US-01).
- International Application No. PCT/US08/067683 filed 20 Jun 2008, which published as WO2009/006046 on 08 Jan 2009 (HHS Reference No. E-219-2007/2-PCT-01).
- U.S. Patent Application No. 12/143,451 filed 20 Jun 2008, which published as U.S. 20090012035 on 08 Jan 2009 (HHS Reference No. E-219-2007/2-US-02).

*Licensing Status:* Available for licensing.

*Licensing Contact:* Cristina Thalhammer-Reyero, PhD, MBA; 301-435-4507; [thalhamc@mail.nih.gov](mailto:thalhamc@mail.nih.gov).

*Collaborative Research Opportunity:* The Laboratory of Bioorganic Chemistry of the National Institute of Diabetes & Digestive & Kidney Diseases is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize dendrimer conjugates of suitably functionalized small molecule ligands of adenosine receptors and P2Y nucleotide receptors. Please contact Dr. Kenneth A. Jacobson at 301-496-9024, or e-mail [kajacobs@helix.nih.gov](mailto:kajacobs@helix.nih.gov), for more information.

Dated: March 19, 2009.

**Richard U. Rodriguez,**

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

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

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#### M2e Peptide Vaccine Against Influenza Virus

*Description of Technology:* The invention offered here is a vaccine candidate that can potentially confer protection against many types of influenza. Current vaccines against influenza virus are comprised of inactivated virus or purified influenza virus proteins and are targeted primarily to induce neutralizing antibodies against the viral hemagglutinin (HA) protein. The virus can mutate or shift antigenic types of HA rapidly rendering the vaccines ineffective and thus the vaccine has to be evaluated yearly to predict next year's circulating strains for vaccine preparation. Unlike HA, the small M2 protein is highly conserved among different strains of influenza virus and thus vaccines based on the M2 protein have the potential to be effective against different strains of influenza. The current invention relates to peptide vaccines composed of the extracellular domain of the M2 protein (M2e) conjugated to a carrier protein. In animals studies a mutant diphtheria toxin-M2e—conjugate induced high antibody levels to both vaccine components in mice.

#### Applications:

- Preventative and therapeutic for influenza virus.
- Vaccine against seasonal and pandemic influenza virus strains.

*Advantages:* Novel vaccine candidate with potential heterosubtypic protection.

*Development Status:* *In vitro* and *in vivo* data can be provided upon request.

*Market:* Influenza virus vaccines.

*Inventors:* Mark A. Miller (FIC), Rachel Schneerson (NICHD), Joanna Kubler-Kielb (NICHD), John B. Robbins (NICHD), Zuzanna Biesova (NICHD), and Jerry Keith (NICHD).

*Patent Status:* U.S. Provisional Application No. 61/089,384 filed 15

Aug 2008 (HHS Reference No. E-304-2008/0-US-01).

*Licensing Status:* Available for licensing.

*Licensing Contact:* Kevin W. Chang, Ph.D.; 301-435-5018; [changke@mail.nih.gov](mailto:changke@mail.nih.gov).

#### Therapeutic HIV Vaccine and Associated Protocols

*Description of Technology:* This technology describes a therapeutic HIV DNA vaccine to be administered to individuals who have previously experienced or are undergoing antiretroviral therapy (ART). The therapeutic DNA vaccine can also be administered in combination with a vector encoding an IL-15 and/or IL-15 receptor alpha (IL-15Ra) polypeptide. In primate studies, the technology was found to be particularly effective when the vaccine composition was administered by electroporation and expressed six (6) HIV antigens (including two (2) gag polypeptides and two (2) envelope polypeptides) and IL-15 and IL-15Ra. The antigens are typically modified with a destabilizing sequence, a secretory polypeptide and/or a degradation signal. Successive administration up to as many as nine resulted in continual boost of the immune response against the encoded antigen. A potent immunotherapeutic vaccine as described here could be an important technology for the fight against HIV/AIDS.

*Applications:* Therapeutic HIV DNA vaccines.

*Development Status:* Primate data available.

*Inventor:* Barbara Felber *et al.* (NCI).

#### Patent Status:

PCT Application No. PCT/US2008/51004 filed 14 Jan 2008, which published as WO 2008/089144 on 24 Jul 2008 (HHS Reference No. E-103-2007/0-PCT-02); claiming priority to 12 Jan 2007.

PCT Application No. PCT/US2007/000774 filed 12 Jan 2007, which published as WO 2007/084342 on 26 Jul 2007 (HHS Reference No. E-254-2005/2-PCT-01); claiming priority to 13 Jan 2006. National Stage filed in AU, BR, CA, CN, EP, IL, IN, JP, MX, NZ, and US.

PCT Application No. PCT/US2001/45624 filed 01 Nov 2001, which published as WO 2002/36806 on 10 May 2002 (HHS Reference No. E-308-2000/0-PCT-02); claiming priority to 01 Nov 2000. National Stage filed in AU, CA, EP, JP, and US.

U.S. Patent Application No. 11/571,879 filed 09 Jan 2007 (HHS Reference No. E-249-2004/1-US-02).

*Licensing Status:* Available for licensing.