

development through collaborative research with the inventors via a Cooperative Research and Development Agreement (CRADA).

#### **Treatment of Human Viral Infections (Imatinib)**

Drs. Steven Zeichner and Vyjayanthi Krishnan (NCI).

U.S. Provisional Application No. 60/588,015 filed 13 Jul 2004 (DHHS Reference No. E-281-2004/0-US-01).

*Licensing Contact:* Sally Hu; 301/435-5606; [hus@mail.nih.gov](mailto:hus@mail.nih.gov).

This application describes the methods for treating or preventing a HIV infection by the administration of *abl*-kinase inhibitor called imatinib and its derivatives. Several available agents can inhibit HIV replication by targeting one or another viral protein, such as the viral reverse transcriptase, protease, envelope fusion process, or integrase, or by targeting the interaction of a viral component with a host cell component, for example the host cell viral receptor or co-receptor. However, HIV can readily become resistant to these drugs, and new therapeutic approaches for HIV infection are needed. The studies described in the application show that the expression of many host cell genes changes in response to HIV replication, and show that targeting one of these changes with imatinib can inhibit viral replication. Thus targeting the host cell, and making the host cell less hospitable to the virus can inhibit viral replication. The application thus describes a new agent that inhibits viral replication by acting on the host cell, which may offer new approaches to therapy for HIV infection. These approaches may be less likely to engender rapid resistance in the virus to the therapy.

This abstract replaces one published in the **Federal Register** on Friday, October 22, 2004 (69 FR 62060).

Dated: December 13, 2004.

**Steven M. Ferguson,**

*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, DHHS.

**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.

#### **AAV4 Vector and Uses Thereof**

John A. Chiorini (NHLBI/NIDCR), Robert M. Kotin (NHLBI), Brian Safer (NHLBI). U.S. Patent 6,468,524 issued 22 Oct 2002 (DHHS Reference No. E-071-2000/0-US-01).

*Licensing Contact:* Jesse Kindra; (301) 435-5559; [kindraj@mail.nih.gov](mailto:kindraj@mail.nih.gov).

The invention described and claimed in this patent application relates to the delivery of heterologous nucleic acids or genes to particular target cells. In particular, the application relates to methods of delivering a heterologous nucleic acid or gene of interest to particular target cells using Adeno-Associated Virus of serotype 4 (AAV4). The particular target cells identified are the ependymal cells of the brain. The methods described herein may be useful in carrying out gene therapy for diseases of the brain or central nervous system.

This work has been published in part at Davidson, BL, *et al.* "Recombinant adeno-associated virus type 2, 4, and 5 vectors: transduction of variant cell types and regions in the mammalian central nervous system" PNAS USA 97(7):3428-32 (March 28, 2000).

In addition, PHS owns additional intellectual property related to this technology describing an AAV4-based vector system. The material contained in the patent application has been published as WO 98/11244 (March 19, 1998) and the research corresponding thereto has been published in J. Virology 71(9): 6823-33 (Sept 1997).

#### **AAV5 Vector for Transducing Brain Cells and Lung Cells**

John A. Chiorini (NHLBI/NIDCR), Robert M. Kotin (NHLBI).

U.S. Patent Application No. 09/533,427 filed 22 Mar 2000 (DHHS Reference No. E-072-2000/0-US-01).

*Licensing Contact:* Jesse Kindra; (301) 435-5559; [kindraj@mail.nih.gov](mailto:kindraj@mail.nih.gov).

The invention described and claimed in this patent application is related to the delivery of heterologous nucleic acids or genes to particular target cells. In particular, the application relates to methods of delivering a heterologous nucleic acid or gene of interest to particular target cells using an Adeno-Associated Virus of serotype 5 (AAV5). The particular target cells identified include the alveolar cells of the lung and cerebellar and ependymal cells of the brain. The methods described herein may be useful in carrying out gene therapy related to diseases of the brain or central nervous system and the respiratory tract.

This work has been published, in part, at Davidson BL, *et al.* PNAS, USA 97(7):3428-32 (March 28, 2000) and Zabner J, *et al.* J Virol. 74(8):3852-8 (April 2000).

In addition to this patent application, PHS owns additional intellectual property related to this technology. The patent application has been published as WO 99/61601 on December 2, 1999 and the research corresponding thereto has been published at Chiorini JA, *et al.* J. Virol. 73(5): 4293-98 (May 1999) and Chiorini JA, *et al.* J. Virol. 73(2): 1309-19 (Feb. 1999).

#### **TTP as a Regulator of GM-CSF mRNA Deadenylation and Stability**

Ester Carballo-Jane, Wi S. Lai, Perry J. Blackshear (NIEHS). U.S. Provisional Application No. 60/148,810 filed 13 Aug 1999 (DHHS Reference No. E-204-1999/0-US-01); PCT Application No. PCT/US00/22199 filed 12 Aug 2000, which published as WO 01/12213 on 22 Feb 2001 (DHHS Reference No. E-204-1999/0-PCT-02); U.S. Patent Application No. 10/049,586 filed 12 Feb 2002 (DHHS Reference No. E-204-1999/0-US-03).

*Licensing Contact:* Jesse Kindra; (301) 435-5559; [kindraj@mail.nih.gov](mailto:kindraj@mail.nih.gov).

The disclosed invention provides materials and methods to treat granulocytopenia (low white cell count in the blood) which is characterized by a reduced number of granulocytes (relative) or an absence of granulocytes (absolute). This condition is commonly associated with cancer chemotherapy, but is seen less frequently in a number of conditions including the use of propylthiouracil, radiotherapy for marrow ablation for bone marrow transplantation, aplastic anemia, systemic lupus erythematosus, AIDS and a variety of other situations. The

invention proposes a method to increase GM-CSF levels in a treated subject, and this increase is achieved by inhibiting the degradation of GM-CSF messenger RNA (mRNA). Tristetraprolin (TTP) is one member of a family of cys-cys-cys-his (CCCCH) zinc finger proteins, and it is a factor that binds to and causes the instability of GM-CSF mRNA. Methods are provided for the development of screening assays for molecules that inhibit the binding of TTP and its related proteins to GM-CSF mRNA, or otherwise inhibit the effect of TTP to promote breakdown of the mRNA, leading in turn to increased mRNA stability and enhanced production of GM-CSF. Compounds identified by such screens, and their derivatives, could be useful in treating granulocytopenia from whatever cause.

Additional information about this technology may be found in the following research articles:

Carballo, E, Lai, WS and Blackshear, PJ. Evidence that tristetraprolin (TTP) is a physiological regulator of granulocyte-macrophage colony-stimulating factor (GM-CSF) mRNA deadenylation and stability. 2000; *Blood* 95:1891–1899.

Lai, WS, Carballo, E, Thorn, JM, Kennington, EA and Blackshear, PJ. Interactions of CCCCH zinc finger proteins with mRNA. 1. Binding of tristetraprolin-related zinc finger proteins to AU-rich elements and destabilization of mRNA. 2000; *J. Biol. Chem.*, 275:17827–19837.

In addition to licensing, the technology is available for further development through collaborative research with the inventors via a Cooperative Research and Development Agreement (CRADA).

Dated: December 13, 2004.

**Steven M. Ferguson,**

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

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#### **The Use of Rabbits With Defined Immunoglobulin Light Chain Genes (C<sub>kappa</sub> b Allotypes) To Optimize Production of Chimeric and Humanized Monoclonal Antibodies for Therapeutic, Imaging and Diagnostic Applications**

Rose G. Mage, Cornelius Alexander (NIAID).

DHHS Reference No. E–332–2004/0—Research Tool.

Licensing Contact: Pradeep Ghosh; (301) 435–5282; [ghoshpr@mail.nih.gov](mailto:ghoshpr@mail.nih.gov).

Biological materials are important research tools that can be used for diagnostic as well as therapeutic purposes. Antibodies have become viable drugs in the market today and there is a general market need for systems that may facilitate production of efficient and effective antibodies. In recent years, monoclonal antibodies have gained significant importance in their use, both as diagnostics and therapeutics, to intervene and combat diseases such as cancer, cardiovascular diseases, and infections. The present invention relates to the discovery of rabbits, genetically defined as b9, as the biological vehicle for the isolation of chimeric phage displaying Fab with human constant regions and rabbit immunoglobulin heavy and light chain variable regions for the development of diagnostic antibodies and humanized monoclonal therapeutic antibodies of high affinity and specificity (Popkov et al., *J. Molec. Biol.* 325: 325–335, 2003; Popkov et al. *J. Immunol. Methods* 288: 149–164, 2004). Recently, many effective antibodies have been developed as a result of the integration of antibody libraries with phage display technology. The rabbit model described in this invention may be used for production of antibodies that may cross react with both human and mouse

antigens. Rabbit monoclonal antibodies that react with both human and mouse antigens are of particular relevance for the preclinical evaluation of therapeutic antibodies in mouse models of human diseases. Therefore, this invention has a broad commercial potential in its use as a source for producing monoclonal antibodies for therapeutic interventions in infectious, autoimmune and neurological diseases, nerve damage and cancer.

#### **Methods for Diagnosis of Atherosclerosis**

Paul Hwang et al. (NHLBI).

U.S. Provisional Application No. 60/607,031 filed 03 Sep 2004 (DHHS Reference No. E–276–2004/0–US–01). Licensing Contact: Fatima Sayyid; (301) 435–4521; [sayyidf@mail.nih.gov](mailto:sayyidf@mail.nih.gov).

In industrialized countries coronary heart disease and stroke due to atherosclerosis are the leading causes of morbidity and mortality. Coronary heart disease is the single largest cause of death in the U.S.A. and will cost approximately \$133.2 billion according to the 2004 American Heart Association statistics update.

The identification of more sensitive and specific markers of atherosclerosis that are non-invasive and cost-effective may have profound impacts on public health. One such strategy involves the detection of marker genes or their products in blood or serum. Such markers may help identify high-risk patients with subclinical atherosclerosis who may benefit from intensive primary prevention or they may help determine the activity of established disease for monitoring response to treatment, resulting in more targeted secondary prevention.

The present invention relates to methods for detecting atherosclerosis using highly reactive biomarkers (FOS and/or DUSP1) expressed in blood cells or released into serum. Because these markers are also involved in pathogenesis, they may serve as potential targets for drug discovery and for intervention to modify disease progression.

#### **An Improved Method To Separate and Expand Antigen-Specific T Cells**

Jonming Li and John Barrett (NHLBI).

U.S. Provisional Application No. 60/606,197 filed 31 Aug 2004 (DHHS Reference No. E–246–2004/0–US–01). Licensing Contact: Fatima Sayyid; (301) 435–4521; [sayyidf@mail.nih.gov](mailto:sayyidf@mail.nih.gov).

Stem cell transplants can be used to treat patients with leukemia or other disorders. Transplanted donor T cells (lymphocytes) exert strong alloimmune