

decrease cell growth and increase sensitivity to standard chemotherapies.

#### Compositions of Matter and Methods of Use of Fluorescent Protein Kinases

Derek Braun and Peter Blumberg (NCI); U.S. Provisional Application filed 19 May 2004 (DHHS Reference No. E-093-2004/0-US-01); Licensing Contact: Mojdeh Bahar; 301/435-2950; [baharm@mail.nih.gov](mailto:baharm@mail.nih.gov).

The invention describes the development of fusion proteins, as well as polynucleotides encoding such fusion proteins, between protein kinase C (PKC) isoforms and variants of green fluorescent protein for the purpose of detecting protein kinase C activation within intact cells via fluorescence resonance energy transfer (FRET). Repeatable dose-dependent change of FRET with a number of PKC ligands, including phorbol esters and bryostatin, have been demonstrated. The invention is useful as a drug discovery tool for evaluating therapeutics that target PKCs.

#### Methods for the Identification and Use of Compounds Suitable for the Treatment of Drug Resistant Cells

Gergely Szakacs *et al.* (NCI); DHHS Reference No. E-075-2004/0-US-01 filed 18 June 2004; Licensing Contact: Jesse S. Kindra; 301-435-5559; [kindraj@mail.nih.gov](mailto:kindraj@mail.nih.gov).

There is an important need to overcome cancer multiple drug resistance (MDR). ATP-binding cassette (ABC) transporters are a family of transporter proteins that contribute to drug resistance via ATP-dependent drug efflux pumps. Accordingly, based on the expression profile of 48 ABC transporters in sixty (60) cell lines, the present invention provides a method to identify (1) drugs that retain action in cells expressing MDR proteins, (2) compounds that reduce MDR by interfering with the efflux pumps. In addition, the invention describes a method to identify compounds whose antiproliferative effect is potentiated by the ABCB1/MDR1 transporter. These compounds might avoid the well-documented side-effects observed in clinical trials of "classical" MDR1 inhibitors and may serve as leads for development of novel anti-cancer agents to treat resistant disease.

#### Methods and Devices for Molecular Diagnosis and Prognosis of Lymphoid Malignancies

Louis M. Staudt *et al.* (NCI); U.S. Provisional Application No. 60/506,377 filed 03 Sep. 2003 (DHHS Reference No. E-234-2003/0-US-01); Licensing Contact: Jeffrey Walenta; 301/435-4633; [walenta@mail.nih.gov](mailto:walenta@mail.nih.gov).

Human lymphomas and leukemias are a diverse set of cancers. Many of these cancers, while expressing a similar phenotype between different individuals, have a diverse underlying genetic basis for the disease. This diverse genetic basis has implications on the effective treatment of the various phenotypes of lymphoma. For example, a drug that was effective against one individual's phenotype of lymphoma will not be effective against a similar lymphoma in another individual. An invention that helps clinicians classify a lymphoproliferative disorder would provide the basis for a "pharmacogenomic" method for treating such cancers.

The patent application listed in this abstract describes the preliminary results of an ongoing effort to establish a molecular basis for classifying all lymphoproliferative disorders. Gene expression profiles, using a gene set of over 27,000 genes, have been established from a large population of lymphoproliferative tumor samples collected from patients at numerous healthcare institutions worldwide. Clinical outcomes were correlated to the gene expression profile data representing a plurality of lymphoid malignancy subtypes of previously known or unknown lymphoproliferative disorders. Finally, an analysis procedure was developed to predict the clinical outcomes based on a patients specific lymphoid tumor gene expression profile.

This patent application describes a method to predict the survival of patient with a lymphoproliferative disorder.

Dated: July 23, 2004.

**Steven M. Ferguson,**

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### National Institutes of Health

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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.

#### Griffithsin, Glycosylation-Resistant Griffithsin, and Related Conjugates, Compositions, Nucleic Acids, Vectors, Host Cells, Methods of Production and Methods of Using

Drs. Barry O'Keefe, Michael Boyd, and Toshiyuki Mori (NCI); U.S. Provisional Application No. 60/576,056 filed 01 Jun 2004 (DHHS Reference No. E-106-2003/0-US-01); Licensing Contact: Sally Hu; 301/435-5606; [hus@mail.nih.gov](mailto:hus@mail.nih.gov).

This invention provides: (1) Isolated and purified antiviral peptides or antiviral proteins named griffithsin; (2) purified nucleic acid encoding griffithsin or a fragment thereof; (3) vectors comprising such a nucleic acid; a host cell comprising such a nucleic acid or vector; (4) a conjugate comprising all or part (such as an antiviral part) of the griffithsin; (5) antibodies that bind griffithsin; (6) methods of producing griffithsin and a conjugate thereof; (7) methods of inhibiting prophylactically and therapeutically a viral infection *e.g.*, HIV, influenza; and, (8) vaccine development and screening assays. Since picomolar concentrations of griffithsin irreversibly inactivate human clinical isolates of HIV and the griffithsin protein can also target other retroviruses (*e.g.* FIV, SIV and HTLV) and non-retroviruses (influenza, measles, ebola) having envelope constituents similar to HIV, this invention may represent potential new therapeutic or prophylactic applications against viruses, including the causative agent for AIDS.

#### Activation of Nerve Growth Factor Receptor Trophic Functions

Lino Tessarollo *et al.* (NCI); U.S. Provisional Application No. 60/509,158 filed 07 Oct 2003 (DHHS Reference No. E-013-2003/0-US-01); Licensing Contact: Norbert Pontzer; 301/435-5502; [pontzern@mail.nih.gov](mailto:pontzern@mail.nih.gov).

Neurotrophins, such as Nerve Growth Factor (NGF), are crucial to the maintenance and survival of neurons of the peripheral and central nervous system. Although these actions have potential therapeutic use in the treatment of a number of neurodegenerative diseases, problems with peripheral administration of these fairly large molecules limits their clinical usefulness. Survival signaling of neurotrophins is mediated mainly through binding to cell surface Trk tyrosine kinase receptors. The juxtamembrane region of the NGF TrkA receptor binds two key adapter proteins, Shc and FRS-2/SNT, which become tyrosine phosphorylated and provide a scaffold for other signaling proteins. The binding of FRS-2/SNT to TrkA is also affected by a neighboring three amino acid KFG domain conserved in all Trk receptors. These inventors found that deletion of the three KFG amino acids affects binding and activation of the adaptor proteins FRS-2/SNT and Shc. This effect increases the general ability to activate downstream TrkA activated signaling pathways in response to NGF. This molecular phenotype leads biologically to a trophic effect on the cholinergic neurons of the basal forebrain and of the striatum *in vivo*. This invention provides a target for selecting small drugs that mimic the effect of KFG domain deletion and thus promote trophic effects in degenerative diseases.

#### **Compositions and Methods for Diagnostics and Therapeutics for Hydrocephalus**

Perry J. Blackshear, Darryl C. Zeldin, Joan P. Graves, Deborah J. Stumpo (NIEHS); U.S. Provisional Patent Application No. 60/374,184 filed 19 Apr 2002 (DHHS Reference No. E-163-2002/0-US-01); U.S. Provisional Patent Application No. 60/388,266 filed 13 Jun 2002 (DHHS Reference No. E-163-2002/1-US-01); PCT Application No. PCT/US03/12348 filed 18 Apr 2003, which published as WO 03/088919 on 30 Oct 2003 (DHHS Reference No. E-163-2002/2-PCT-01); Licensing Contact: Pradeep Ghosh; 301/435-5282; [ghoshpr@mail.nih.gov](mailto:ghoshpr@mail.nih.gov).

Congenital hydrocephalus is a public health problem and a significant population suffers from this birth defect in the United States. It has been estimated that a significant number of patients with congenital hydrocephalus also suffer from aqueductal stenosis. Congenital hydrocephalus has an adverse effect on developing brain and may persist as neurological defects in children and adults. Some of these defects may manifest in form of mental

retardation, cerebral palsy, epilepsy and visual disabilities. The cost of treatment for such disorders may exceed \$100 million annually. Efficient diagnostics to determine the risks of development of hydrocephalus are lacking in the market.

This invention relates to RFX4\_v3 proteins and nucleic acids encoding the RFX4\_v3 proteins. RFX4\_v3 proteins are associated with congenital hydrocephalus. Congenital hydrocephalus is a common birth defect and many cases of hydrocephalus are caused by chromosome X-linked genetic mutations. The present invention provides assays for the detection of RFX4\_v3 polymorphisms associated with congenital hydrocephalus that may lead to the determination of an individual's risk of developing disease states and conditions. Therefore, the present invention would be most useful in developing diagnostic tests for abnormalities that may lead to the development of hydrocephalus and thus, has a market potential of substantial significance.

Dated: July 23, 2004.

#### **Steven M. Ferguson,**

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496-7057; fax: (301) 402-0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

#### **Monoclonal Antibody (MP804) That Specifically Binds Stem Cells and Its Use**

Neal D. Epstein (NHLBI); U.S. Provisional Application No. 60/565,101 filed 23 Apr 2004 (DHHS Reference No. E-014-2004/0-US-01); Licensing Contact: Fatima Sayyid; (301) 435-4521; [sayyidf@mail.nih.gov](mailto:sayyidf@mail.nih.gov).

Adult stem cells hold great promise for human disorders that are currently incurable including spinal-cord injury and brain diseases. Although it has been shown that adult stem cells can produce many different tissue types in the body, from blood to muscle to nerve leading hope to their use for repairing or replacing diseased or damaged organs, their use is limited due to lack of reagents for isolation of adult stem cells from tissues. This invention is drawn to antibodies that can detect a subpopulation of primitive stem cells in adult murine skeletal muscle. This subset of cells can be used to repair a variety of neurological disorders, to produce primary and immortalized cell lines for physiologic and pharmaceutical research, and for genomic and proteomic studies focused on the process of neural cell differentiation.

#### **Modulating P38 Kinase Activity**

Dr. Jonathan Ashwell (NCI); U.S. Provisional Application No. 60/541,993 filed 05 Feb 2004 (DHHS Reference No. E-010-2004/0-US-01); Licensing Contact: Marlene Shinn-Astor; (301) 435-4426; [shinnm@mail.nih.gov](mailto:shinnm@mail.nih.gov).

Protein kinases are involved in various cellular responses to extracellular signals. The protein kinase termed p38 is also known as cytokine suppressive anti-inflammatory drug binding protein (CSBP) and RK. It is believed that p38 has a role in mediating cellular response to inflammatory stimuli, such as leukocyte accumulation, macrophage/monocyte activation, tissue resorption, fever, acute phase responses and neutrophilia. In addition, p38 has been implicated in cancer, thrombin-induced platelet aggregation, immunodeficiency disorders, autoimmune diseases, cell death, allergies, osteoporosis and neurodegenerative disorders.

The NIH announces a new technology that includes compositions and methods for controlling the activity of p38 specifically in T cells through an alternate activation pathway. By controlling p38 activity through