invention discloses a device and method for improving the accuracy of fluorescence spot counting. This has been accomplished mainly through the following improvements: (1) A method to analyze ratios of test and reference spot signals in a field of view, (2) an imaging system to acquire confocal images to cells to provide a set of different layers of the same cells, at different positions along the Z-axis, and (3) a software program to make use of the three-dimensional nature of the images, which makes the identification of FISH signals more accurate. Licensing of an algorithm for automated FISH spot counting is recommended for manufacturers of scientific and medical instrumentation and in particular for manufacturers of commercial imaging devices as well as companies that specialize in providing fluorescent probes for molecular biology research.

Licensing of Applications of Tissue Microarrays

(4) NIH Reference No. E–007–99/0 (USSN 60/106,038, PCT/US99/04000), entitled ''Tissue Microarrays for Rapid Molecular Profiling'', originally filed 10/28/98, PCT filed 02/24/99. Inventors: O. Kallioniemi, G. Sauter and J. Kononen.

(5) NIH Reference No. E–274–99/0 (USSN 60/171,262), entitled ''Methods of Making and Using Microarrays'', filed 12/15/99. Inventors: O. Kallionemi and G. Sauter.

These two inventions disclose methods of using tissue microarrays for a wide variety of clinical applications. E–007–99/0 describes in great detail high-throughput screening studies of thousands of tissue samples. These studies, ordinarily requiring many days to perform, can be completed in only a few hours when tissue microarrays are used. Licensees of this invention will be able to manufacture tissue microarrays using clinical samples and distribute the panels and companion reagents to the medical and research community. Commercially produced microarrays could be developed for use as reference standards for certain diseases or custom made for specific needs.

E–274–99/0 describes the use of tissue microarrays for educational, standardization and OC (histological test kits) purposes. With respect to the first proposed use, licensees will be able, for example, to distribute microarray panels and companion reagents in medical teaching institutions. With respect to the latter two uses, standard microrray panels could be included in clinical test kits that are histological (IHC or ISH) procedures.

Tissue Microarray technology and its applications have been described in several publications, such as Nature Medicine 4:844 (1998), Cancer Research 59:803 (1999), J Natl Cancer Inst. 91:1758 (1999), Clin Cancer Res 5:1966 (1999), J Natl Cancer Inst, 92:1252 (2000).

Dated: October 6, 2000.

Jack Spiegel,

Director, Division of Technology Development and Transfer, Office of Technology Transfer.

[FR Doc. 00–27355 Filed 10–24–00; 8:45 am]

BILLING CODE 4140–01–M

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 agencies 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.

A Cultured Cell Line which Expresses the GLU4 Glucose Transporter Isoform Labeled with a Short Hemaglutinin Peptide and a Modified Green Fluorescence Protein

Samuel W. Cushman (NIDDK), DHHS Reference No. E–264–00/0 filed 26 Jul 2000; Licensing Contact: Marlene Shinn; 301/496–7056 ext. 285; email: shinnm@od.nih.gov.

The aforementioned invention is currently available through a Biological Materials License as a research tool. Insulin regulates glucose uptake by inducing the translocation of GLUT4, a glucose transporter isoform expressed in fat and muscle, from intracellular components to the plasma membrane. The NIH announces the discovery of a cell line that expresses the GLUT4 glucose transporter isoform with a short hemaglutin peptide (HA) and a modified green fluorescent protein (GFP). The HA peptide is recognized by a specific antibody when GLUT4 is in the plasma membrane but not when GLUT4 is sequestered inside the cell. The modified GFP can be detected by its fluorescence whether it is inside the cell or on the cell surface. This allows the HA label to quantitate the GLUT4 subcellular distribution and the GFP label, the total GLUT4 expression. Therefore, this invention can be used in high through-put screening, as an assay reagent, and it may aid specifically in ascertaining compounds that have the insulin-like effect of stimulating GLU4 translocation from an intracellular compartment to the cell surface.

Dmt-tic Di- and Tri-Peptidic Derivatives and Related Compositions and Methods of Use

Lawrence H. Lazarus (NIEHS), DHHS Reference No. E–103–00/0 filed 24 Mar 2000; Licensing Contact: Marlene Shinn; 301/496–7056 ext. 285; e-mail: shinnm@od.nih.gov.

A major obstacle in the treatment of many cancers involves the clinical manifestation of drug resistance. Currently, toxic substances are used in clinical and therapeutic settings to inhibit glycoproteins in the cell membrane of some cancer cells that have the ability to pump out of the cell drugs that would be potentially lethal. The most common of these glycoproteins is the 170-kd ATP-dependent transmembrane efflux pump. The multidrug resistance (MDR1) phenotype, however, is not the sole source of drug resistance since MDR1 is a member of a superfamily of proteins structurally related to the transmembrane P-glycoproteins.

NIH scientists have prepared a series of δ-opiod analogs of Dmt-tic (2′,6′-dimethyl-L-tyrosine-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid). At least one of the analogs, which is biologically stable and exerts no known side effects, has been observed to inhibit the ability of MDR1 to pump out a fluorescent probe from the cell membrane. Thus, these analogs might represent novel chemosensitizing agents to treat both hematologic malignancies (lymphomas) and solid tumors (e.g. breast and colon) without toxic effects in patients.

In addition, this invention provides more potent δ-opioid antagonists and δ-opiod antagonists with duel binding

affinity and biological activity toward δ-opiod and μ-opiod receptors. These compounds therefore, have the potential to treat opiate and alcohol abuse, neurological diseases, neuropeptide or neurotransmitter imbalances, neurological and immune dysfunction, graft rejections through immunosuppression with antagonists, pain control through short half-life agonists, and shock and brain injuries.

Scratch Wound Assay Device

Katherine Malinda et al. (NINR), Serial No. 09/496,134 filed 01 Feb 2000; Licensing Contact: Dale Berkley; 301/496–7735 ext. 223; e-mail: berkleyd@od.nih.gov.

Tissue wounds undergo a complex and ordered series of events to repair tissue. These events may include infiltration of inflammatory immune cells as part of the process to remove and destroy necrotic tissue, increased vascularization by angiogenic factors, and increased cell proliferation and extracellular matrix deposition. Although the basic process of tissue repair has been characterized, the individual steps and factors necessary to carry out this complex series of events are not yet well understood or fully identified. Accordingly, there is a need to develop a way of reproducibly injuring a layer of cells to study the effects of different compounds of treatments on the ability of the remaining cells to repair the damaged area.

The present invention provides a device that reproducibly makes a wound of a desired size in a cell layer grown on a cell culture material. The device allows researchers to use small volumes of cells and test materials suggesting its use as a tool in high throughput screening of compounds. This provides researchers with a faster, more accurate way of screening large numbers of factors and determining the effects of cell growth and migration agents in model wounds produced in the cell, organ, or tissue layer.

Method of in vitro T cell Differentiation of CD34+ Progenitor Cells

Ruiz et al. (NIAID), DHHS Reference No. E–206–98/0 filed 29 Oct 1999; Licensing Contact: J. P. Kim; 301/496–7056 ext. 264; e-mail: kimj@od.nih.gov.

The present invention relates to a human in vitro system for inducing the growth and de novo differentiation of T cells from CD34+ progenitor cells in the presence of various cytokine cocktails and lymph node stroma. The mature T cells which are generated may be used to treat individuals with primary or acquired T cell immunodeficiencies, including HIV infection.

Dated: October 13, 2000.

Jack Spiegel,

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.

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A Plasmid for Expression of a Soluble Form of HIV–1 Integrase Protein

Robert Craigie et al. (NIDDK), NIH Reference No. E–108–00/0; Licensing Contact: J.P. Kim; 301/496–7056 ext. 264; e-mail: kimj@od.nih.gov.

Integrase is an essential HIV enzyme and a promising target for antiviral therapy. Integrase protein is required to assay for inhibitors of this enzyme and for mechanistic studies on HIV DNA integration. Further, drugs targeted to integrase would provide a new therapeutic approach to the treatment of AIDS and could be used in combination therapy with drugs that target RT and protease. The subject plasmid can be used to produce large quantities of a soluble form of HIV–1 integrase protein for such work.

TTP as a Regulator of GM–CSF mRNA Deadenylation and Stability

Ester Carballo-Jane, Wi S. Lai, Perry J. Blackshear (NIEHS), NIH Reference No. E–204–99/0 filed 13 Aug 1999; Licensing Contact: Vasant Gandhi; 301/496–7056 ext. 244; e-mail: gandhiv@od.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 (CCCH) 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.

Novel Post-Transcriptional Regulatory Elements and Uses Thereof

George N. Pavlakis and Filomena Nappi (NCI), NIH Reference Nos. E–143–98/0 filed 22 May 1998 and E–143–98/1 filed 22 May 1999; Licensing Contact: Carol Salata; 301/496–7735 ext. 232; e-mail: salatac@od.nih.gov.

This invention concerns a novel post-transcriptional regulatory element that can function as an RNA nucleo-cytoplasmic transport element (NCTE) and its use to make recombinant attenuated HIV strains useful as vaccines. HIV regulates its expression by controlling the nuclear transport of unspliced mRNA encoding structural proteins. HIV utilizes the Rev/RRE system. RRE (Rev responsible element) is an HIV encoded NCTE, which is part of every HIV RNA encoding the